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     (FILE 'HOME' ENTERED AT 13:03:58 ON 18 MAR 2001)
               SET COST OFF

     FILE 'HCAPLUS' ENTERED AT 13:04:07 ON 18 MAR 2001
                 E SELDEN R/AU
L1            56 S E3,E5,E8-E10
                 E TRECO D/AU
L2            33 S E3-E7
                 E MILLER A/AU
L3           387 S E3,E32,E87,E88,E148,E155,E156
L4           455 S L1-L3
                 E MRNA/CW
L5         29996 S E3
                 E MRNA/CT
                 E E3+ALL
L6         61949 S E6,E7
L7         31841 S E5+NT
L8            88 S E15
L9           122 S E14
                 E E4+ALL
L10       125315 S E5
L11       148840 S E4+NT
L12        69018 S E64+NT OR E65+NT OR E66+NT OR E67+NT OR E68+NT OR E69+NT
L13           13 S L4 AND L5-L12
L14            8 S L4 AND ?MRNA?
L15            5 S L4 AND MESSENGER(L)(RNA OR RIBONUCLE?)
L16           20 S L13-L15
L17            2 S L4 AND FACTOR VIII

     FILE 'REGISTRY' ENTERED AT 13:11:53 ON 18 MAR 2001
L18            1 S 9001-27-8

     FILE 'HCAPLUS' ENTERED AT 13:12:11 ON 18 MAR 2001
L19            1 S L18 AND L4
L20            2 S L17,L19
L21           22 S L16,L20
L22           18 S L1 AND L2,L3
L23            3 S L2 AND L3
L24            1 S L22 AND L23
L25           23 S L21,L24
L26            7 S L22,L23 AND L25
L27           23 S L25,L26
L28           13 S L22,L23 NOT L27
L29            6 S CODON AND L4
                 E CODON/CT
                 E E3+ALL
L30         5789 S E1,E2
                 E E2+ALL
L31         3981 S E3+NT
L32            4 S L4 AND L30,L31
L33            5 S L29,L32 AND L21-L28
L34            6 S L20,L33

     FILE 'BIOSIS' ENTERED AT 13:21:57 ON 18 MAR 2001
                 E MILLER A/AU
L35          993 S E3,E34
                 E MILLER ALLAN/AU
L36            4 S E3,E5
                 E TRECO D/AU
L37           24 S E3-E6
                 E SELDEN R/AU
L38           68 S E3,E5,E6,E9,E10
L39         1076 S L35-L38
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L40           2 S L39 AND CODON
L41           3 S L39 AND CODING
L42          12 S L39 AND ENCOD?
L43          15 S L40-L42
L44          20 S L39 AND (MRNA OR RNA OR RIBONUCLE? OR RIBO NUCLE?)
L45          91 S L39 AND (10052 OR 10062)/CC
L46          92 S L44,L45
L47         401 S L39 AND 00520/CC
L48         420 S L39 AND CONFERENCE/DT
L49         491 S L39 AND (CONGRESS OR POSTER OR SYMPOS? OR MEETING OR ASSEMBLY
L50          32 S L49 NOT L47,L48
L51          10 S L50 AND (CONGRESS OR SYMPOS? OR CONFERENCE OR MEETING)/SO
L52         470 S L47,L48,L51
L53          34 S L52 AND L46
L54          34 S L52 AND L40-L46
L55          34 S L53,L54

     FILE 'HCAPLUS' ENTERED AT 13:32:15 ON 18 MAR 2001
L56          37 S L21-L29,L34

=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 13:32:47 ON 18 MAR 2001
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FILE COVERS 1967 - 18 Mar 2001  VOL 134 ISS 13
FILE LAST UPDATED: 16 Mar 2001  (20010316/ED)

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this searchable data in CAOLD.  You now have electronic access to all
of CA: 1907 to 1966 in CAOLD and 1967 to the present in HCAPLUS on STN.


=> d 156 bib abs hitrn tot


L56  ANSWER 1 OF 37  HCAPLUS  COPYRIGHT 2001 ACS
AN   2000:646120  HCAPLUS
DN   133:234455
TI   Methods for modification of .alpha.-galactosidase A glycosylation, for
     purification of enzyme, and for treatment of Fabry disease
IN   Selden, Richard F.; Borowski, Marianne; Kinoshita, Carol M.;
     Treco, Douglas A.; Williams, Melanie D.; Schuetz, Thomas J.;
     Daniel, Peter F.
PA   Transkaryotic Therapies, Inc., USA
SO   PCT Int. Appl., 92 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
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| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2000053730 | A2 | 20000914 | WO 2000-US6118 | 20000309 |

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1999-266014 19990311

AB The invention provides highly purified .alpha.-galactosidase A (.alpha.-Gal A), and various methods for purifying it; .alpha.-Gal A prepns. with altered charge and methods for making those prepns.; .alpha.-Gal A prepns. that have an extended circulating half-life in a mammalian host, and methods for making same; and methods and dosages for administering an .alpha.-Gal A prepn. to a subject. Thus, using Bu Sepharose, Heparin Sepharose, hydroxyapatite, Q Sepharose, and Superdex 200 column chromatog., .alpha.-Gal A was purified, in 59% yield, to a specific activity of 2.92 X 106 units/mg protein. The glycosylation pattern of the enzyme was altered by enzymic treatment (e.g., with sialidase) and its biodistribution detd. Desialylated .alpha.-Gal A localized more to the liver than did the untreated enzyme. Fabry fibroblast cocultured with recombinant fibroblast secreting .alpha.-Gal A internalized the enzyme and exhibited .alpha.-Gal A activity similar to that of normal cells.

L56 ANSWER 2 OF 37 HCAPLUS COPYRIGHT 2001 ACS
AN 2000:454242 HCAPLUS
DN 133:53716
TI Gene and enzyme replacement therapy for .alpha.-galactosidase A deficiency
IN **Selden, Richard F.**; Borowski, Marianne; Gillispie, Frances P.; Kinoshita, Carol M.; **Treco, Douglas A.**; Williams, Melanie D.
PA Transkaryotic Therapies, Inc., USA
SO U.S., 32 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 6083725 | A | 20000704 | US 1997-928881 | 19970912 |

PRAI US 1996-26041 19960913

AB A therepeutic method whereby an individual suspected of having an .alpha.-galactosidase A deficiency, such as Fabry disease, is treated either with (1) human cells that have been genetically modified to overexpress and secrete human .alpha.-gal A, or (2) purified human .alpha.-gal A obtained from cultured, genetically modified human cells. A therapeutic method is provided whereby an individual suspected of having an .alpha.-galactosidase A (.alpha.-gal A) deficiency, such as Fabry disease, is treated either with (1) human cells that have been genetically modified to overexpress and secrete human .alpha.-gal A, or (2) purified human .alpha.-gal A obtained from cultured, genetically modified human cells. Expressing a DNA encoding human .alpha.-gal A in cultured human cells produces a polypeptide that is glycosylated appropriately, so that it is not only enzymically active and capable of acting on the glycosphingolipid substrate which accumulates in Fabry disease, but is also efficiently internalized by cells via cell surface receptors which target it exactly to where it is needed in this disease. Two expression plasmids, pXAG-16 and pXAG-28, were constructed. These plasmids contain human .alpha.-gal A cDNA encoding the 398 amino acids of the .alpha.-gal A enzyme (without its signal peptide); the human growth hormone (hGH) signal peptide genomic DNA sequence, which is interrupted by the first intron of the hGH gene; and the 3'-untranslated sequence (UTS) of the hGH gene,

which contains a signal for polyadenylation. Plasmid pXAG-16 has the human cytomegalovirus immediate-early promoter and first intron (flanked by noncoding exon sequences), whereas pXAG-28 is driven by the collagen I.alpha.2 promoter and also contains the .beta.-actin gene's 5'-UTS, which contains the first intron of the .beta.-actin gene. Expression by fibroblasts stably transfected with pXAG-16 or pXAG-28, using the hGH signal peptide, was substantially higher than that in transfected fibroblasts using the homologous .alpha.-gal A signal peptide. Recombinant .alpha.-gal A could be purified by Butyl-Sepharose hydrophobic interaction chromatog., heparin-Sepharose chromatog., hydroxylapatite chromatog., Q Sepharose HP anion-exchange chromatog., and Superdex-200 gel filtration chromatog. Purified .alpha.-Gal A activity was stable over a 3-mo period when the pH of the formulation was <6.5.

RE.CNT 25
RE
(2) Anon; EP 0307285 1989 HCAPLUS
(3) Anon; WO 9011353 1990 HCAPLUS
(4) Anon; WO 9309222 1993 HCAPLUS
(5) Anon; WO 9412628 1994 HCAPLUS
(6) Anon; WO 9506478 1995 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 3 OF 37 HCAPLUS COPYRIGHT 2001 ACS
AN 2000:238012 HCAPLUS
DN 132:247163
TI In vivo protein production and delivery system for gene therapy
IN **Selden, Richard F.**; **Treco, Douglas**; Heartlein, Michael W.
PA Transkaryotic Therapies, Inc., USA
SO U.S., 26 pp., Cont.-in-part of U.S. Ser. No. 312,444, abandoned. CODEN: USXXAM
DT Patent
LA English
FAN.CNT 8

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 6048729 | A | 20000411 | US 1994-334797 | 19941104 |
| | AU 8817160 | A1 | 19881202 | AU 1988-17160 | 19880502 |
| | AU 632457 | B2 | 19930107 | | |
| | JP 02503265 | T2 | 19901011 | JP 1988-504046 | 19880502 |
| | DK 8905447 | A | 19891229 | DK 1989-5447 | 19891101 |
| | US 6054288 | A | 20000425 | US 1995-443936 | 19950518 |
| PRAI | US 1987-44719 | | 19870501 | | |
| | US 1991-787760 | | 19911106 | | |
| | US 1992-918927 | | 19920722 | | |
| | US 1994-180701 | | 19940113 | | |
| | US 1994-312444 | | 19940926 | | |
| | WO 1988-US1448 | | 19880502 | | |
| | US 1991-787840 | | 19911105 | | |
| | US 1994-334797 | | 19941104 | | |

AB The present invention relates to transfected primary and secondary somatic cells of vertebrate origin, particularly mammalian origin, transfected with exogenous genetic material (DNA) which encodes a desired (e.g., a therapeutic) product or is itself a desired (e.g., therapeutic) product, methods by which primary and secondary cells are transfected to include exogenous genetic material, methods of producing clonal cell strains or heterogeneous cell strains, methods of gene therapy in which the transfected primary or secondary cells are used, and methods of producing antibodies using the transfected primary or secondary cells. The present invention includes primary and secondary somatic cells, such as fibroblasts, keratinocytes, epithelial cells, endothelial cells, glial cells, neural cells, formed elements of the blood, muscle cells, other somatic cells which can be cultured and somatic cell precursors, which have been transfected with exogenous DNA which is stably integrated into their genomes or is expressed in the cells episomally. The exogenous DNA either encodes a product, such as a translational product (e.g., a

protein) or a transcriptional product (e.g., a ribozyme or an anti-sense nucleic acid sequence) which is a therapeutic product or is itself a therapeutic product (e.g., DNA which binds to a cellular regulatory protein or alters gene expression).

RE.CNT 169

RE

(1) Aebischer; US 4892538 1990 HCAPLUS
(3) Anderson; US 5399346 1995 HCAPLUS
(4) Anon; EP 0038765 1981 HCAPLUS
(5) Anon; EP 0038765 B 1981 HCAPLUS
(7) Anon; EP 0236059 1987 HCAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 4 OF 37 HCAPLUS COPYRIGHT 2001 ACS
AN 2000:38523 HCAPLUS
DN 132:189638
TI Infusion of .alpha.-galactosidase A reduces tissue globotriaosylceramide storage in patients with Fabry disease
AU Schiffmann, R.; Murray, G. J.; **Treco, D.**; Daniel, P.; Sellos-Moura, M.; Myers, M.; Quirk, J. M.; Zirzow, G. C.; Borowski, M.; Loveday, K.; Anderson, T.; Gillespie, F.; Oliver, K. L.; Jeffries, N. O.; Doo, E.; Liang, T. J.; Kreps, C.; Gunter, K.; Frei, K.; Crutchfield, K.; **Selden, R. F.**; Brady, R. O.
CS Developmental and Metabolic Neurology Branch, National Institute of Neurological Disorders and Stroke, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD, 20892-1260, USA
SO Proc. Natl. Acad. Sci. U. S. A. (2000), 97(1), 365-370
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
AB Fabry disease is a lysosomal storage disorder caused by a deficiency of the lysosomal enzyme .alpha.-galactosidase A (.alpha.-gal A). This enzymic defect results in the accumulation of the glycosphingolipid globotriaosylceramide (Gb3; also referred to as ceramidetrihexoside) throughout the body. To investigate the effects of purified .alpha.-gal A, 10 patients with Fabry disease received a single i.v. infusion of one of five escalating dose levels of the enzyme. The objectives of this study were: (i) to evaluate the safety of administered .alpha.-gal A, (ii) to assess the pharmacokinetics of i.v.-administered .alpha.-gal A in plasma and liver, and (iii) to det. the effect of this replacement enzyme on hepatic, urine sediment and plasma concns. of Gb3. .alpha.-Gal A infusions were well tolerated in all patients. Immunohistochem. staining of liver tissue approx. 2 days after enzyme infusion identified .alpha.-gal A in several cell types, including sinusoidal endothelial cells, Kupffer cells, and hepatocytes, suggesting diffuse uptake via the mannose 6-phosphate receptor. The tissue half-life in the liver was greater than 24 h. After the single dose of .alpha.-gal A, nine of the 10 patients had significantly reduced Gb3 levels both in the liver and shed renal tubular epithelial cells in the urine sediment. These data demonstrate that single infusions of .alpha.-gal A prepd. from transfected human fibroblasts are both safe and biochem. active in patients with Fabry disease. The degree of substrate redn. seen in the study is potentially clin. significant in view of the fact that Gb3 burden in Fabry patients increases gradually over decades. Taken together, these results suggest that enzyme replacement is likely to be an effective therapy for patients with this metabolic disorder.

RE.CNT 28

RE

(6) Crawley, A; J Clin Invest 1996, V97, P1864 HCAPLUS
(11) Gross, S; Anal Biochem 1980, V102, P429 HCAPLUS
(13) Hille-Rehfeld, A; Biochim Biophys Acta 1995, V1241, P177 HCAPLUS
(14) Hozumi, I; J Lipid Res 1990, V31, P335 HCAPLUS
(15) Humes, H; Miner Electrolyte Metab 1995, V21, P353 HCAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 5 OF 37 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:723191 HCAPLUS
DN 131:347493
TI Genomic sequences upstream of the coding region of the interferon-.alpha.2 gene IFNA2 for protein production and delivery
IN **Treco, Douglas A.**; Heartlein, Michael W.; **Selden, Richard F.**
PA Transkaryotic Therapies, Inc., USA
SO PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9957292 | A1 | 19991111 | WO 1999-US9925 | 19990505 |
| | W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| | AU 9937888 | A1 | 19991123 | AU 1999-37888 | 19990505 |
| | EP 1075531 | A1 | 20010214 | EP 1999-920375 | 19990505 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| | NO 2000005585 | A | 20010105 | NO 2000-5585 | 20001106 |

PRAI US 1998-84648 19980507
US 1998-86555 19980521
WO 1999-US9925 19990505
AB The present invention is based upon the identification and sequencing of genomic DNA upstream of the coding region of the human interferon-.alpha.2 (IFNA2) gene. This DNA can be used, for example, in a DNA construct that alters (e.g., increases) expression of an endogenous IFNA2 gene in a mammalian cell upon integration into the genome of the cell via homologous recombination.
RE.CNT 7
RE
(1) Geisel, C; EMBL DATABASE ENTRY AC004081 1998
(2) Geisel, C; UNPUBLISHED
(3) Heartlein Michael W; US 5641670 A HCAPLUS
(4) Heartlein Michael W; WO 9531560 A 1995 HCAPLUS
(5) Lawn, R; PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE USA 1981, V78(9) HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 6 OF 37 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:723190 HCAPLUS
DN 131:347492
TI Genomic sequences upstream of the coding region of the G-CSF gene for protein production and delivery
IN **Treco, Douglas A.**; Heartlein, Michael W.; **Selden, Richard F.**
PA Transkaryotic Therapies, Inc., USA
SO PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9957291 | A1 | 19991111 | WO 1999-US9924 | 19990505 |

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

| | | | | | |
|---|---|---|---|---|---|
| AU | 9937887 | A1 | 19991123 | AU 1999-37887 | 19990505 |
| EP | 1075530 | A1 | 20010214 | EP 1999-920374 | 19990505 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| NO | 2000005586 | A | 20010103 | NO 2000-5586 | 20001106 |

PRAI US 1998-84649 19980507
WO 1999-US9924 19990505

AB The present invention is based upon the identification and sequencing of genomic DNA upstream of the coding region of the human granulocyte colony-stimulating factor (G-CSF) gene. This DNA can be used, for example, in a DNA construct that alters (e.g., increases) expression of an endogenous G-CSF gene in a mammalian cell upon integration into the genome of the cell via homologous recombination.

RE.CNT 3
RE
(1) Heartlein Michael W; US 5641670 A HCAPLUS
(2) Heartlein Michael W; WO 9531560 A 1995 HCAPLUS
(3) Kershaw, J; no publication given 1996

L56 ANSWER 7 OF 37 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:723162 HCAPLUS
DN 131:332968
TI sequence and modification of expression of human FSH beta gene by homologous recombination and therapeutic implications for reproductive disorders
IN **Treco, Douglas A.**; Heartlein, Michael W.; **Selden, Richard F.**
PA Transkaryotic Therapies, Inc., USA
SO PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9957263 | A1 | 19991111 | WO 1999-US9795 | 19990505 |
| | W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| | AU 9938817 | A1 | 19991123 | AU 1999-38817 | 19990505 |
| | EP 1075514 | A1 | 20010214 | EP 1999-921670 | 19990505 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| | US 6200778 | B1 | 20010313 | US 1999-305639 | 19990505 |
| | NO 2000005587 | A | 20010103 | NO 2000-5587 | 20001106 |

PRAI US 1998-84663 19980507
WO 1999-US9795 19990505

AB An isolated nucleic acid mol. that hybridizes under stringent conditions, or shares at least 80 % sequence identity, with a defined genomic region upstream of the coding region of a FSH.beta. gene, and a DNA construct contg. that nucleic acid mol. as a targeting sequence for homologous

recombination. FSH is a gonadotrophin which plays an essential role in the maintenance and development of oocytes and spermatozoa in normal reproductive physiol. This method is aimed at altering gene expression in a mammalian cell by targeting a regulatory sequence or exon or splice site or intron or CAP site for inactivation by recombination. Effective delivery methods of FSH.beta. to cells are described where cells secrete FSH.beta.. This method likewise has applications for gene therapy for reproductive disorders.

RE.CNT 6
RE
(1) Anon; DATABASE EMMAM 1990
(3) Applied Research Systems Ars Holding N V; US 5272071 A 1993 HCAPLUS
(4) Genzyme Corporation; US 5639640 A 1997 HCAPLUS
(5) Hirai; JOURNAL OF MOLECULAR ENDOCRINOLOGY 1990, V5, P147 HCAPLUS
(6) Transkaryotic Therapies Inc; US 5641670 A 1997 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 8 OF 37 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:708908 HCAPLUS
DN 131:318576
TI Delivery of **Factor VIII**, Factor IX, or other therapeutic proteins via implantation of genetically modified cells in the omentum, and uses thereof in the treatment of coagulation and thrombosis disorders
IN Lamsa, Justin Chase; **Treco, Douglas A.**
PA Transkaryotic Therapies, Inc., USA
SO PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9955866 | A1 | 19991104 | WO 1999-US8266 | 19990416 |
| | W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| | AU 9934944 | A1 | 19991116 | AU 1999-34944 | 19990416 |
| | EP 1071768 | A1 | 20010131 | EP 1999-916683 | 19990416 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI | | | | |

PRAI US 1998-82982 19980424
WO 1999-US8266 19990416

AB The invention provides a method of expressing therapeutic proteins, such as clotting factors, in a mammal by introducing a genetically modified cell into the omentum. The method of the invention allows for long-term systemic delivery of a protein of interest to a mammal for the prevention or treatment of disorders assocd. with coagulation and thrombosis. Preferably, the protein of interest is a **Factor VIII** or IX clotting factor, and thus, the invention provides methods and means for treating/preventing hemophilia.

IT **9001-27-8P, Factor VIII**
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(delivery of **Factor VIII**, Factor IX, or other therapeutic proteins via implantation of genetically modified cells in the omentum, and uses thereof in the treatment of coagulation and thrombosis disorders)

RE.CNT 7
RE

(1) Chuah; HUMAN GENE THERAPY 1998, V9(3), P353 HCAPLUS
(2) Dwarki, V; PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA 1995, V92(4), P1023 HCAPLUS
(4) Moullier, P; NATURE MEDICINE 1995, V1(4), P353 HCAPLUS
(5) Transkaryotic Therapies Inc; WO 9309222 A 1993 HCAPLUS
(6) Univ Duke; WO 9815615 A 1998 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 9 OF 37 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:207287 HCAPLUS
DN 128:279556
TI Formation of high-level expression cassettes by directed integration of transforming DNA and the manufacture of therapeutic proteins
IN **Treco, Douglas A.**; Heartlein, Michael W.; Hauge, Brian M.; **Selden, Richard F.**
PA Transkaryotic Therapies, Inc., USA
SO U.S., 50 pp. Cont.-in-part of U.S. 5,641,670.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 8

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 5733746 | A | 19980331 | US 1995-406030 | 19950317 |
| | EP 750044 | A2 | 19961227 | EP 1996-202037 | 19921105 |
| | EP 750044 | A3 | 19970115 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE | | | | |
| | US 6063630 | A | 20000516 | US 1994-231439 | 19940420 |
| | US 5641670 | A | 19970624 | US 1994-243391 | 19940513 |
| | US 6187305 | B1 | 20010213 | US 1995-446921 | 19950518 |
| | US 6048524 | A | 20000411 | US 1995-446909 | 19950522 |
| | US 6048724 | A | 20000411 | US 1995-446911 | 19950522 |
| | CA 2215618 | AA | 19960926 | CA 1996-2215618 | 19960312 |
| | WO 9629411 | A1 | 19960926 | WO 1996-US3377 | 19960312 |
| | W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI | | | | |
| | RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN | | | | |
| | AU 9653625 | A1 | 19961008 | AU 1996-53625 | 19960312 |
| | AU 725832 | B2 | 20001019 | | |
| | EP 815232 | A1 | 19980107 | EP 1996-910432 | 19960312 |
| | R: DE, FR, GB | | | | |
| | JP 11502122 | T2 | 19990223 | JP 1996-528475 | 19960312 |
| | ZA 9602116 | A | 19961003 | ZA 1996-2116 | 19960315 |

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|---|---|---|
| PRAI | US 1991-787840 | 19911105 |
| | US 1991-789188 | 19911105 |
| | US 1992-911533 | 19920710 |
| | US 1992-985586 | 19921203 |
| | US 1994-243391 | 19940513 |
| | EP 1992-924367 | 19921105 |
| | US 1994-231439 | 19940420 |
| | US 1994-334455 | 19941104 |
| | US 1995-406030 | 19950317 |
| | WO 1996-US3377 | 19960312 |

AB A method for achieving high level expression of therapeutically useful genes by directed integration of transforming DNA that increases the level of expression of the endogenous gene is described. The transforming DNA is a targeting construct that includes least: a targeting sequence; a regulatory sequence; an exon; and a splice-donor site. Integration of the transforming DNA by homologous recombination at the desired site leads to formation a an expression construct with a strong promoter and 5'-intron/exon construct that leads to efficient expression and and processing of the gene product. The transforming DNA may also contain a selectable marker that may be an amplifiable gene such as the

dihydrofolate reductase gene. The method is particularly intended for proteins of known therapeutic use: thrombopoietin, DNase I, or .beta.-interferon.

L56 ANSWER 10 OF 37 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:183999 HCAPLUS
DN 128:239483
TI Gene and enzyme replacement therapy for .alpha.-galactosidase A deficiency
IN **Selden, Richard F.**; Borowski, Marianne; Gillespie, Frances P.; Kinoshita, Carol M.; **Treco, Douglas A.**; Williams, Melanie D.
PA Transkaryotic Therapies, Inc., USA; Selden, Richard F.; Borowski, Marianne; Gillespie, Frances P.; Kinoshita, Carol M.; Treco, Douglas A.; Williams, Melanie D.
SO PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 9811206 | A2 | 19980319 | WO 1997-US16603 | 19970912 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9744244 | A1 | 19980402 | AU 1997-44244 | 19970912 |
| EP 935651 | A2 | 19990818 | EP 1997-942567 | 19970912 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| CN 1230220 | A | 19990929 | CN 1997-197909 | 19970912 |
| NO 9901225 | A | 19990510 | NO 1999-1225 | 19990312 |

PRAI US 1996-712614 19960913
WO 1997-US16603 19970912

AB A therapeutic method is provided whereby an individual suspected of having an .alpha.-galactosidase A (.alpha.-gal A) deficiency, such as Fabry disease, is treated either with (1) human cells that have been genetically modified to overexpress and secrete human .alpha.-gal A, or (2) purified human .alpha.-gal A obtained from cultured, genetically modified human cells. Expressing a DNA encoding human .alpha.-gal A in cultured human cells produces a polypeptide that is glycosylated appropriately, so that it is not only enzymically active and capable of acting on the glycosphingolipid substrate which accumulates in Fabry disease, but is also efficiently internalized by cells via cell surface receptors which target it exactly to where it is needed in this disease. Two expression plasmids, pXAG-16 and pXAG-28, were constructed. These plasmids contain human .alpha.-gal A cDNA encoding the 398 amino acids of the .alpha.-gal A enzyme (without its signal peptide); the human growth hormone (hGH) signal peptide genomic DNA sequence, which is interrupted by the first intron of the hGH gene; and the 3'-untranslated sequence (UTS) of the hGH gene, which contains a signal for polyadenylation. Plasmid pXAG-16 has the human cytomegalovirus immediate-early promoter and first intron (flanked by noncoding exon sequences), whereas pXAG-28 is driven by the collagen I.alpha.2 promoter and also contains the .beta.-actin gene's 5'-UTS, which contains the first intron of the .beta.-actin gene. Expression by fibroblasts stably transfected with pXAG-16 or pXAG-28, using the hGH signal peptide, was substantially higher than that in transfected fibroblasts using the homologous .alpha.-gal A signal peptide. Recombinant .alpha.-gal A could be purified by Butyl-Sepharose hydrophobic interaction chromatog., heparin-Sepharose chromatog., hydroxylapatite chromatog., Q Sepharose HP anion-exchange chromatog., and Superdex-200 gel filtration chromatog. Purified .alpha.-Gal A activity was stable over a 3-mo period when the pH of the formulation was <6.5.

L56 ANSWER 11 OF 37 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:425951 HCAPLUS
DN 127:91349
TI Protein production and protein delivery
IN **Treco, Douglas A.**; Heartlein, Michael W.; **Selden, Richard F.**
PA Transkaryotic Therapies, Inc., USA
SO U.S., 50 pp. Cont.-in-part of U.S. Ser. No. 985,586, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 8

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 5641670 | A | 19970624 | US 1994-243391 | 19940513 |
| | EP 750044 | A2 | 19961227 | EP 1996-202037 | 19921105 |
| | EP 750044 | A3 | 19970115 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE | | | | |
| | US 6063630 | A | 20000516 | US 1994-231439 | 19940420 |
| | CN 1119545 | A | 19960403 | CN 1994-107587 | 19940602 |
| | US 5733746 | A | 19980331 | US 1995-406030 | 19950317 |
| | CA 2190289 | AA | 19951123 | CA 1995-2190289 | 19950511 |
| | WO 9531560 | A1 | 19951123 | WO 1995-US6045 | 19950511 |
| | W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT | | | | |
| | RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| | AU 9525504 | A1 | 19951205 | AU 1995-25504 | 19950511 |
| | AU 709058 | B2 | 19990819 | | |
| | EP 759082 | A1 | 19970226 | EP 1995-919831 | 19950511 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| | BR 9507874 | A | 19970819 | BR 1995-7874 | 19950511 |
| | HU 76844 | A2 | 19971128 | HU 1996-3144 | 19950511 |
| | JP 10500570 | T2 | 19980120 | JP 1995-529826 | 19950511 |
| | ZA 9503879 | A | 19960118 | ZA 1995-3879 | 19950512 |
| | US 6187305 | B1 | 20010213 | US 1995-446921 | 19950518 |
| | US 6048524 | A | 20000411 | US 1995-446909 | 19950522 |
| | US 6048724 | A | 20000411 | US 1995-446911 | 19950522 |
| | US 5733761 | A | 19980331 | US 1995-451893 | 19950526 |
| | US 5968502 | A | 19991019 | US 1995-451894 | 19950526 |
| | FI 9604536 | A | 19970109 | FI 1996-4536 | 19961112 |
| | NO 9604802 | A | 19970109 | NO 1996-4802 | 19961112 |

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|---|---|---|
| PRAI | US 1991-787840 | 19911105 |
| | US 1991-789188 | 19911105 |
| | US 1992-911533 | 19920710 |
| | US 1992-985586 | 19921203 |
| | EP 1992-924367 | 19921105 |
| | US 1994-231439 | 19940420 |
| | US 1994-243391 | 19940513 |
| | US 1994-334455 | 19941104 |
| | WO 1995-US6045 | 19950511 |

AB The invention relates to constructs comprising: a) a targeting sequence; b) a regulatory sequence; c) an exon; and d) an unpaired splice-donor site. The invention further relates to a method of producing protein in vitro or in vivo comprising the homologous recombination of a construct as described above within a cell. The homologously recombinant cell is then maintained under conditions which will permit transcription and translation, resulting in protein expression. The present invention further relates to homologously recombinant cells, including primary, secondary, or immortalized vertebrate cells, methods of making the cells, methods of homologous recombination to produce fusion genes, methods of altering gene expression in the cells, and methods of making a protein in

a cell employing the constructs of the invention.

L56 ANSWER 12 OF 37 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:173241 HCAPLUS
DN 126:250004
TI Lipoxygenase metabolism is required for interleukin-3 dependent proliferation and cell cycle progression of the human M-07e cell line
AU **Miller, Alan M.**; Allen, Beverly Steele; Ziboh, Vincent
CS Tulane Cancer Center, Tulane University, New Orleans, LA, 70112, USA
SO J. Cell. Physiol. (1997), 170(3), 309-315
CODEN: JCLLAX; ISSN: 0021-9541
PB Wiley-Liss
DT Journal
LA English
AB The cell line M-07e requires either interleukin-3 (IL-3) or granulocyte-macrophage colony stimulating factor (GM-CSF) for proliferation in vitro. Cells deprived of growth factor for up to 48 h remain viable but no longer divide. The growth-factor-deprived M-07e cells begin to divide within 48 h of reexposure to IL-3. Flow cytometric anal. of M-07e cells labeled with hypotonic propidium iodide demonstrates that the percentage of cells undergoing DNA synthesis decreases from 24%, in a log phase population of IL-3 stimulated cells, to 1% when cells are deprived of IL-3 for 24 h. IL-3-deprived cells accumulate predominantly in a flow cytometry peak representative of G0/G1. DNA synthetic activity, as detd. by tritiated thymidine uptake and flow cytometry, resumes between 12 and 18 h after reexposure to IL-3, reaching a peak of up to 40% by 24 h and returning to log phase levels by 72 h. Prior to initiation of DNA synthesis, increases are seen in **mRNA** levels for 5-lipoxygenase-activating protein (FLAP). Following reexposure to IL-3, a rapid time-dependent biosynthesis of leukotriene D4 (LTD4) is induced by M-07e cells. When IL-3 is added in the presence of any of three lipoxygenase inhibitors tested (Piriprost, caffeic acid, nordihydroguiaretic acid) or FLAP inhibitor, MK-886, there is dose-dependent inhibition of the resumption of proliferation and of DNA synthesis. Flow cytometric cell cycle anal. demonstrates that the inhibited cells remain in the G0/G1 population and do not progress through the cell cycle. These results are consistent with the authors previous observation that an intact lipoxygenase pathway is necessary for hematopoietic growth-factor-stimulated colony formation of normal bone marrow myeloid progenitors and suggest that the induction of a lipoxygenase metabolite or metabolites is necessary for myeloid cells to progress through the cell cycle when stimulated by a hematopoietic growth factor.

L56 ANSWER 13 OF 37 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:721777 HCAPLUS
DN 126:2480
TI Thrombopoietin, DNase I, or .beta.-interferon gene therapy, targeting sequences for homologous recombination, and treatment of platelet disorder, cystic fibrosis, or multiple sclerosis
IN **Treco, Douglas A.**; Heartlein, Michael W.; Hauge, Brian M.; **Selden, Richard F.**
PA Transkaryotic Therapies, Inc., USA
SO PCT Int. Appl., 114 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 8

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 9629411 | A1 | 19960926 | WO 1996-US3377 | 19960312 |

W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,

IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN

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|---|---|---|---|---|---|
| US | 5733746 | A | 19980331 | US 1995-406030 | 19950317 |
| AU | 9653625 | A1 | 19961008 | AU 1996-53625 | 19960312 |
| AU | 725832 | B2 | 20001019 | | |
| EP | 815232 | A1 | 19980107 | EP 1996-910432 | 19960312 |
| | R: DE, FR, GB | | | | |
| JP | 11502122 | T2 | 19990223 | JP 1996-528475 | 19960312 |
| PRAI | US 1995-406030 | 19950317 | | | |
| | US 1991-787840 | 19911105 | | | |
| | US 1991-789188 | 19911105 | | | |
| | US 1992-911533 | 19920710 | | | |
| | US 1992-985586 | 19921203 | | | |
| | US 1994-243391 | 19940513 | | | |
| | WO 1996-US3377 | 19960312 | | | |

AB The invention relates to novel human DNA sequences, targeting constructs, and methods for producing novel genes encoding thrombopoietin DNase I and .beta.-interferon by homologous recombination. The targeting constructs comprise at least: (a) a targeting sequence; (b) a regulatory sequence; (c) an exon; and (d) a splice-donor site. The targeting constructs, which can undergo homologous recombination with endogenous cellular sequences to generate a novel gene, are introduced into cells to produce homologously recombinant cells. The homologously recombinant cells are then maintained under conditions which will permit transcription of the novel gene and translation of the **mRNA** produced, resulting in prodn. of either thrombopoietin, DNase I, or .beta.-interferon. The invention further relates to methods of producing pharmaceutically useful prepns. contg. thrombopoietin, DNase I or .beta.-interferon from homologously recombinant cells and methods of gene therapy comprising administering homologously recombinant cells producing thrombopoietin, DNase I, or .beta.pinterferon to a patient for therapeutic prospects.

L56 ANSWER 14 OF 37 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:58252 HCAPLUS
DN 124:78726
TI DNA construct for effecting homologous recombination and uses for recombinant protein production
IN **Treco, Douglas A.**; Heartlein, Michael W.; **Selden, Richard F.**
PA Transkaryotic Therapies, Inc., USA
SO PCT Int. Appl., 147 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 8

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9531560 | A1 | 19951123 | WO 1995-US6045 | 19950511 |
| | W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT | | | | |
| | RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| | US 5641670 | A | 19970624 | US 1994-243391 | 19940513 |
| | CN 1119545 | A | 19960403 | CN 1994-107587 | 19940602 |
| | AU 9525504 | A1 | 19951205 | AU 1995-25504 | 19950511 |
| | AU 709058 | B2 | 19990819 | | |
| | EP 759082 | A1 | 19970226 | EP 1995-919831 | 19950511 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| | BR 9507874 | A | 19970819 | BR 1995-7874 | 19950511 |
| | JP 10500570 | T2 | 19980120 | JP 1995-529826 | 19950511 |
| | FI 9604536 | A | 19970109 | FI 1996-4536 | 19961112 |
| | NO 9604802 | A | 19970109 | NO 1996-4802 | 19961112 |
| PRAI | US 1994-243391 | 19940513 | | | |
| | US 1991-787840 | 19911105 | | | |

US 1991-789188 19911105
US 1992-911533 19920710
US 1992-985586 19921203
WO 1995-US6045 19950511

AB The invention relates to constructs comprising: a) a targeting sequence; b) a regulatory sequence; c) an exon; and d) an unpaired splice-donor site. The invention further relates to a method of producing protein in vitro or in vivo comprising the homologous recombination of a construct as described above within the cell. The homologously recombinant cell is then maintained under conditions which will permit transcription and transition, resulting in protein expression. The present invention further relates to homologously recombinant cells, including primary, secondary, or immortalized vertebrate cells, methods of making the cells, methods of homologous recombination to produce fusion genes, methods of altering gene expression in the cells, and methods of making a protein in a cell employing the constructs of the invention.

L56 ANSWER 15 OF 37 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:7631 HCAPLUS
DN 124:105277
TI Non-viral gene therapy
AU **Treco, Douglas A; Selden, Richard F**
CS TKT Incorporated, Cambridge, MA, 02139, USA
SO Mol. Med. Today (1995), 1(7), 314-21
CODEN: MMTOFK; ISSN: 1357-4310
DT Journal; General Review
LA English
AB A review with 39 refs. Gene therapy is a medical/surgical intervention currently being developed, in which genes are introduced into cells in order to treat or cure a wide variety of human diseases. The field has evolved over the past four decades, with most exptl. gene-therapy studies based on the use of viruses to deliver the genes of therapeutic interest. More recently, a large no. of non-viral approaches to gene therapy have emerged, yielding promising pre-clin. results, and which are currently being evaluated in early stage clin. trials.

L56 ANSWER 16 OF 37 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:534392 HCAPLUS
DN 122:281145
TI Fibroblast cell biology and gene therapy
AU **Treco, Douglas A.**; Heartlein, Michael W.; **Selden, Richard F**
CS Transkaryotic Therapies, Inc., Cambridge, MA, USA
SO Somatic Gene Ther. (1995), 49-60. Editor(s): Chang, Patricia L. Publisher: CRC, Boca Raton, Fla.
CODEN: 61EAAZ
DT Conference; General Review
LA English
AB A review with 52 refs. In vitro approaches to fibroblast engineering and gene therapy are considered.

L56 ANSWER 17 OF 37 HCAPLUS COPYRIGHT 2001 ACS
AN 1994:693220 HCAPLUS
DN 121:293220
TI Long-term production and delivery of human growth hormone in vivo
AU Heartlein, Michael W.; Roman, Victoria A.; Jiang, Ji-Lei; Sellers, Joan W.; Zuliani, Antoinette M.; **Treco, Douglas A.**; **Selden, Richard F.**
CS TKT, Inc., Cambridge, MA, 02139, USA
SO Proc. Natl. Acad. Sci. U. S. A. (1994), 91(23), 10967-71
CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English
AB The application of somatic cell gene therapy to large patient populations will require the development of safe and practical approaches to the generation and characterization of genetically manipulated cells.

Transkaryotic implantation is a gene therapy system based on the prodn. of clonal strains of engineered primary and secondary cells, using nonviral methods. We demonstrate here that, on implantation, these clonal cell strains stably and reproducibly deliver pharmacol. quantities of protein for the lifetime of the exptl. animals.

L56 ANSWER 18 OF 37 HCAPLUS COPYRIGHT 2001 ACS
AN 1994:527071 HCAPLUS
DN 121:127071
TI Activating expression of an amplifying endogenous gene by homologous recombination
IN **Treco, Douglas A.**; Heartlein, Michael W.; **Selden, Richard F.**
PA Transkaryotic Therapies, Inc., USA
SO PCT Int. Appl., 93 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 8

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 9412650 | A2 | 19940609 | WO 1993-US11704 | 19931202 |
| WO 9412650 | A3 | 19940804 | | |
| W: AU, CA, JP, KR, NZ | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| CA 2151032 | AA | 19940609 | CA 1993-2151032 | 19931202 |
| AU 9457362 | A1 | 19940622 | AU 1994-57362 | 19931202 |
| AU 689455 | B2 | 19980402 | | |
| EP 672160 | A1 | 19950920 | EP 1994-903405 | 19931202 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| AU 9858401 | A1 | 19980604 | AU 1998-58401 | 19980312 |
| AU 726446 | B2 | 20001109 | | |

PRAI US 1992-985586 19921203
WO 1993-US11704 19931202

AB A method method is described for activating expression of and amplifying an endogenous gene in genomic DNA of a vertebrate cell which is not expressed in the cell as obtained or is not expressed at significant levels in the cell as obtained. The method includes transfecting cells with DNA sequences comprising (1) exogenous DNA sequences which repair, alter, delete, or replace a sequence present in the cell or which are regulatory sequences not normally functionally linked to the endogenous gene in the cell as obtained, (2) DNA sequences homologous with genomic DNA sequences at a preselected site in the cells, and (3) amplifiable DNA encoding a selectable marker. The cells are maintained under conditions appropriate for homologous recombination to occur between DNA sequences homologous with genomic DNA sequences and genomic DNA sequences. The homologously recombinant cells are cultured under conditions which select from amplification of the amplifiable DNA encoding a selectable marker, whereby the amplifiable DNA encoding a selectable marker and the endogenous gene functionally linked to exogenous DNA are coamplified. Thus, the method activates expression of endogenous cellular genes and further allows amplification of the activated endogenous cellular genes but does not require in vitro manipulation and transfection of exogenous DNA encoding proteins of therapeutic interest. Homologous recombination can also be used to convert a gene into a cDNA copy (devoid of introns) which can then be transferred into yeast, bacteria, or mammalian cells for in vitro protein prodn. Transfected primary, secondary, and immortalized cells were transfected by homologous recombination to activate endogenous genes in ways desirable for in vitro protein prodn. (e.g., pharmaceuticals) or in vivo protein delivery methods (e.g., gene therapy). Two strategies are presented in detail for transcriptionally activating the hEPO gene.

L56 ANSWER 19 OF 37 HCAPLUS COPYRIGHT 2001 ACS
AN 1994:236973 HCAPLUS
DN 120:236973

TI Hematopoietic growth factor induction of gamma-glutamyl transferase in the KG-I myeloid cell line
AU **Miller, Alan M.**; Sandler, Eric; Kobb, Steven M.; Eastgate, Julie; Zucali, James
CS Div. Med. Oncol., Coll. Med., Gainesville, FL, USA
SO Exp. Hematol. (Charlottesville, Va.) (1993), 21(1), 9-15
CODEN: EXHMA6; ISSN: 0301-472X
DT Journal
LA English
AB The ability of hematopoietic growth factors (HGF) to induce gamma-glutamyl transferase (GGT) enzyme activity and **mRNA** content was examd. in a HGF-responsive cell line (KG-1). Incubation of KG-1 with recombinant human cytokines interleukin-1.beta. (IL-1.beta.), interleukin-3 (IL-3), granulocyte-macrophage CSF (GM-CSF), and tumor necrosis factor (TNF), but not interleukin-6 (IL-6), granulocyte CSF (G-CSF) or monocyte CSF (M-CSF), results in significant increases in GGT enzyme activity. The increases in GGT activity are both dose- and time-dependent. In response to IL-1, increases in enzyme activity are seen by 6 h and activity is maximal by 24 h. GGT **mRNA** increases also occur and peak by 3-6 h. Apparently, induction of increases in GGT **mRNA** levels and enzyme activity occur in myeloid cells in response to HGFs. This induction, together with the requirement for LTD4 for normal granulopoiesis, supports a role for GGT in the cellular events occurring in myeloid cells in response to HGFs.

L56 ANSWER 20 OF 37 HCAPLUS COPYRIGHT 2001 ACS
AN 1993:574980 HCAPLUS
DN 119:174980
TI Recombination walking: Genetic selection of clones from pooled libraries of yeast artificial chromosomes by homologous recombination
AU **Miller, Allan M.**; Savinelli, Elizabeth A.; Couture, Sandra M.; Hannigan, Gene M.; Han, Zhiyi; **Selden, Richard F.**; **Treco, Douglas A.**
CS Transkaryotic Ther., Inc., Cambridge, MA, 02139, USA
SO Proc. Natl. Acad. Sci. U. S. A. (1993), 90(17), 8118-22
CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English
AB Recombination walking is based on the genetic selection of specific human clones from a yeast artificial chromosome (YAC) library by homologous recombination. The desired clone is selected from a pooled (unordered) YAC library, eliminating labor-intensive steps typically used in organizing and maintaining ordered YAC libraries. Recombination walking represents an efficient approach to library screening and is well suited for chromosome-walking approaches to the isolation of genes assocd. with common diseases.

L56 ANSWER 21 OF 37 HCAPLUS COPYRIGHT 2001 ACS
AN 1993:532007 HCAPLUS
DN 119:132007
TI Adaptation to supraphysiologic levels of insulin gene expression in transgenic mice: Evidence for the importance of posttranscriptional regulation
AU Schnetzler, Bruno; Murakawa, George; Abalos, Deborah; Halban, Philippe; **Selden, Richard**
CS Lab. Rech. Louis Jeantet, Cent. Med. Univ., Geneva, 1211, Switz.
SO J. Clin. Invest. (1993), 92(1), 272-80
CODEN: JCINAO; ISSN: 0021-9738
DT Journal
LA English
AB Insulin prodn. was studied in transgenic mice expressing the human insulin gene under the control of its own promoter. Glucose homeostasis during a 48-h fast was similar in control and transgenic mice, with comparable levels of serum immunoreactive insulin. Northern blot and primer extension anal. indicated that more than twice as much insulin **mRNA** is present in pancreata from transgenic mice. Primer

extension anal. using oligonucleotides specific for mouse insulins I and II or for human insulin, showed that the excess insulin **mRNA** was due solely to expression of the foreign, human insulin gene. The ratio of **mRNA** for mouse insulin I and II was unaffected by coexpression of human insulin. There were coordinate changes in the levels of all three **mRNA** during the 48-h fast, or after a 24-h fast followed by 24-h refeed. Despite the supraphysiol. levels of insulin **mRNA** in the transgenic mice, their pancreatic content of immunoreactive insulin was not different from controls. The comparison of the relative levels of human and mouse insulin **mRNAs** with their peptide counterparts (sepd. by HPLC) indicates that the efficiency of insulin prodn. from mouse insulin **mRNA** is greater than that from human, stressing the importance of posttranscriptional regulatory events in the overall maintenance of pancreatic insulin content.

L56 ANSWER 22 OF 37 HCAPLUS COPYRIGHT 2001 ACS
AN 1993:442724 HCAPLUS
DN 119:42724
TI Transgenic vertebrate cells producing therapeutic product and their use in gene therapy
IN **Selden, Richard F.**; Heartlein, Michael W.; **Treco, Douglas A.**
PA Transkaryotic Therapies, Inc., USA
SO PCT Int. Appl., 151 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 8

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9309222 | A2 | 19930513 | WO 1992-US9627 | 19921105 |
| | WO 9309222 | A3 | 19931028 | | |
| | W: AU, CA, JP, KR | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE | | | | |
| | AU 9230698 | A1 | 19930607 | AU 1992-30698 | 19921105 |
| | AU 669499 | B2 | 19960613 | | |
| | JP 07500969 | T2 | 19950202 | JP 1992-508767 | 19921105 |
| | EP 649464 | A1 | 19950426 | EP 1992-924367 | 19921105 |
| | EP 649464 | B1 | 19970723 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE | | | | |
| | EP 750044 | A2 | 19961227 | EP 1996-202037 | 19921105 |
| | EP 750044 | A3 | 19970115 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE | | | | |
| | AT 155810 | E | 19970815 | AT 1992-924367 | 19921105 |
| | ES 2106891 | T3 | 19971116 | ES 1992-924367 | 19921105 |
| | US 6063630 | A | 20000516 | US 1994-231439 | 19940420 |
| | US 5994127 | A | 19991130 | US 1994-334455 | 19941104 |
| | US 6187305 | B1 | 20010213 | US 1995-446921 | 19950518 |
| | US 6048524 | A | 20000411 | US 1995-446909 | 19950522 |
| | US 6048724 | A | 20000411 | US 1995-446911 | 19950522 |
| | AU 9665631 | A1 | 19961128 | AU 1996-65631 | 19960913 |
| | AU 710255 | B2 | 19990916 | | |

PRAI US 1991-787840 19911105
US 1991-789188 19911105
US 1992-911533 19920710
EP 1992-924367 19921105
WO 1992-US9627 19921105
US 1994-231439 19940420
US 1994-334455 19941104

AB Primary and secondary cells of vertebrates, esp. mammals, are transfected with exogenous DNA encoding a therapeutic product (e.g., erythropoietin, human growth hormone). The transgenic cells produce the encoded therapeutic product stably and reproducibly, both in vitro and in vivo, over extended periods of time. Addnl., the trangenic cells express the product in vivo at physiol. relevant levels; they are recoverable after implantation; and, the recovered cells, upon reculturing, grow and display

their preimplantation properties.

L56 ANSWER 23 OF 37 HCAPLUS COPYRIGHT 2001 ACS
AN 1993:162446 HCAPLUS
DN 118:162446
TI Screening of DNA libraries in eukaryotic hosts using homologous recombination
IN **Treco, Douglas A.; Miller, Allan M.**
PA Transkaryotic Therapies, Inc., USA
SO PCT Int. Appl., 126 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9303183 | A1 | 19930218 | WO 1991-US8679 | 19911121 |
| | W: AU, CA, JP, KR | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE | | | | |
| | AU 9212781 | A1 | 19930302 | AU 1992-12781 | 19911121 |
| | EP 596885 | A1 | 19940518 | EP 1992-905456 | 19911121 |
| | EP 596885 | B1 | 19970903 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| | JP 06508983 | T2 | 19941013 | JP 1991-505202 | 19911121 |
| | AT 157708 | E | 19970915 | AT 1992-905456 | 19911121 |
| | US 5580734 | A | 19961203 | US 1994-301872 | 19940906 |
| | US 5869239 | A | 19990209 | US 1995-443372 | 19950517 |
| | AU 9662112 | A1 | 19961205 | AU 1996-62112 | 19960815 |
| | AU 693712 | B2 | 19980702 | | |

PRAI US 1991-739861 19910802
US 1990-552183 19900713
WO 1991-US8679 19911121
US 1994-301872 19940906

AB A method of screening a DNA library in an eukaryotic host that makes use of homologous recombination between a probe carrying a selectable marker and a target sequence is described. The host carrying the library is transformed with a non-replicating DNA fragment carrying the target sequence flanking the selectable marker. After allowing homologous recombination to take place the bank is selected for cells retaining the selectable marker. The preferred host for this method is Saccharomyces cerevisiae or Schizosaccharomyces pombe. A no. of YAC vectors for this use are described. The use of the method to identify a no. of human genes in a YAC bank is described.

L56 ANSWER 24 OF 37 HCAPLUS COPYRIGHT 2001 ACS
AN 1992:122639 HCAPLUS
DN 116:122639
TI Homologous recombination method for identifying and isolating DNA fragments from DNA libraries in eukaryotic cells
IN **Treco, Douglas A.; Miller, Allan M.**
PA Transkaryotic Therapies, Inc., USA
SO PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9201069 | A1 | 19920123 | WO 1991-US4926 | 19910712 |
| | W: AU, CA, JP, KR | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE | | | | |
| | CA 2086092 | AA | 19920114 | CA 1991-2086092 | 19910712 |
| | AU 9182991 | A1 | 19920204 | AU 1991-82991 | 19910712 |
| | EP 539490 | A1 | 19930505 | EP 1991-913696 | 19910712 |
| | EP 539490 | B1 | 19951108 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |

| | | | | | |
|---|---|---|---|---|---|
| | JP 05508547 | T2 | 19931202 | JP 1991-513075 | 19910712 |
| | AT 130049 | E | 19951115 | AT 1991-913696 | 19910712 |
| | ES 2080957 | T3 | 19960216 | ES 1991-913696 | 19910712 |
| | US 5580734 | A | 19961203 | US 1994-301872 | 19940906 |
| | US 5783385 | A | 19980721 | US 1994-300919 | 19940906 |
| | US 5869239 | A | 19990209 | US 1995-443372 | 19950517 |
| | AU 9644493 | A1 | 19960620 | AU 1996-44493 | 19960212 |
| | AU 689015 | B2 | 19980319 | | |
| PRAI | US 1990-552183 | 19900713 | | | |
| | WO 1991-US4926 | 19910712 | | | |
| | US 1991-739861 | 19910802 | | | |
| | US 1994-301872 | 19940906 | | | |

AB A method for selecting DNA fragments in an eukaryotic host by forced integration of a selectable marker into the sequence of interest is described. A DNA fragment carrying a selectable marker and a sequence long enough to direct homologous recombination to take place is introduced into the host carrying the bank. The bank is selected for stable transformants carrying the marker. This method is useful for chromosome walking and genetic mapping. It allows screening for many specific sequences simultaneously and storage of libraries as a pool of clones rather than as individuals; and it speeds up the library screening process. The method was illustrated using yeast ARG4- contg. DNA from human white blood cells on YACs carrying the selectable markers TRP1 and URA3. Targeting plasmid p184DLARG contg. the yeast ARG4 gene and a bacterial origin of replication was prepd. and a DNA fragment contg. the 5' flanking region of the .epsilon.-globin gene was inserted into it. Clones contg. the desired globin sequences were identified by growth on medium lacking uracil, tryptophan, and arginine.

L56 ANSWER 25 OF 37 HCAPLUS COPYRIGHT 2001 ACS
AN 1990:546674 HCAPLUS
DN 113:146674
TI The human growth hormone transgene: expression in hemizygous and homozygous mice
AU Yun, Jeung S.; Li, Yunsheng; Wight, David C.; Portanova, Ronald; **Selden, Richard F.**; Wagner, Thomas E.
CS Coll. Osteopath. Med., Ohio Univ., Athens, OH, 45701, USA
SO Proc. Soc. Exp. Biol. Med. (1990), 194(4), 308-13
CODEN: PSEBAA; ISSN: 0037-9727
DT Journal
LA English
AB Female transgenic mice carrying the mouse metallothionein-1/human growth hormone (hGH) fusion gene are sterile. Transmission of the transgene has been limited to the male germ line, resulting in the prodn. of hemizygous (He) progeny contg. only a single (paternal) copy of the gene. Using ovary transfer, the authors developed procedures for producing homozygous (Ho) TG mice, viz., male TG mice were mated with control (non-TG) females carrying ovaries donated by female TG mice. In both He and Ho TG animals, serum levels of hGH were higher (1.5-fold) in males than in females, tended to decrease with age of the animal, and were increased (about 5-fold) by zinc induction. However, in comparison to He animals of the same sex, the Ho TG mice attained a greater body wt. and had more than 2-fold higher levels of liver hGH **mRNA** and serum hGH, both under basal conditions and in response to zinc induction. I.e., the expression of the transgene was qual. similar to He and Ho TG mice, but the level of transgene activity was greater in the Ho animals. Apparently, indicate that both copies (maternal and paternal) of the transgene were active and expressed additively (or cooperatively) in the Ho TG animal.

L56 ANSWER 26 OF 37 HCAPLUS COPYRIGHT 2001 ACS
AN 1989:628806 HCAPLUS
DN 111:228806
TI Mating-type control in Saccharomyces cerevisiae: isolation and characterization of mutants defective in repression by a1-.alpha.2
AU Harashima, Satoshi; **Miller, Allan M.**; Tanaka, Kazuma; Kusumoto, Kenichi; Tanaka, Kohichi; Mukai, Yukio; Nasmyth, Kim; Oshima, Yasuji

CS Fac. Eng., Osaka Univ., Suita, 565, Japan
SO Mol. Cell. Biol. (1989), 9(10), 4523-30
CODEN: MCEBD4; ISSN: 0270-7306
DT Journal
LA English
AB The .alpha.2 protein, the product of the MAT.alpha.2 cistron, represses various genes specific to the a mating type (.alpha.2 repression), and when combined with MATa1 gene product, it represses MAT.alpha.1 and various haploid-specific genes (a1-.alpha.2 repression). One target of a1-.alpha.2 repression is RME1, which is a neg. regulator of a/.alpha.-specific genes. Thirteen recessive mutants were isolated whose a1-.alpha.2 repression is defective but which retain .alpha.2 repression in a genetic background of ho MATa HML.alpha. HMRa sir3 or ho MAT.alpha. HMRa HMRa sir3. These mutations can be divided into 3 different classes. One class contains a missense mutation, designated hml.alpha.2-102, in the .alpha.2 cistron of HML, and another class contains 2 missense mutations, mat.alpha.2-201 and mat.alpha.2-202, in the MAT.alpha. locus. These 3 mutants each have an amino acid substitution of tyrosine or phenylalanine for cysteine at the 33rd **codon** from the translation initiation **codon** in the .alpha.2 cistron of HML.alpha. or MAT.alpha.. The remaining 10 mutants make up the 3rd class and form a single complementation group, having mutations designated aar1 (a1-.alpha.2 repression), at a gene other than MAT, HML, HMR, RME1, or the 4 SIR genes. Although a diploid cell homozygous for the aar1 and sir3 mutations and for the MATa, HML.alpha., and HMRa alleles showed .alpha. mating type, it could sporulate and give rise to asci contg. 4 .alpha. mating-type spores. These facts indicate that the domain for .alpha.2 repression is separable from that for a1-.alpha.2 protein interaction or complex formation in the .alpha.2 protein and that an addnl. regulatory gene, AAR1, is assocd. with the a1-.alpha.2 repression of the .alpha.1 cistron and haploid-specific genes.

L56 ANSWER 27 OF 37 HCAPLUS COPYRIGHT 2001 ACS
AN 1989:451506 HCAPLUS
DN 111:51506
TI Glucocorticoid regulation of human growth hormone expression in transgenic mice and transiently transfected cells
AU **Selden, R. F.**; Yun, J. S.; Moore, D. D.; Rowe, M. E.; Malia, M. A.; Wagner, T. E.; Goodman, H. M.
CS Dep. Mol. Biol., Massachusetts Gen. Hosp., Boston, MA, 02114, USA
SO J. Endocrinol. (1989), 122(1), 49-60
CODEN: JOENAK; ISSN: 0022-0795
DT Journal
LA English
AB A mouse metallothionein-I/human growth hormone fusion gene was microinjected into fertilized mouse eggs, the embryos were implanted into pseudopregnant foster mothers, and the offspring analyzed. Five of 26 mice born after 1 series of injections contained from 1 to 8 copies of the fusion gene stably integrated into their genomes and had human growth hormone in their serum. When several of these transgenic mice and transgenic offspring were treated with glucocorticoids, serum growth hormone levels were elevated 1.5-6.3-fold. A 4-fold induction in fusion gene **mRNA** in the liver of one of the 5 mice was also obsd. after treatment with glucocorticoids. When the fusion gene was transiently transfected into mouse L cells, dexamethasone caused a 3-4-fold induction of fusion gene **mRNA** and secreted human growth hormone. A deletion anal. of regulatory elements required for inducibility in L cells shows that DNA sequences responsible for the obsd. inductions are located within the transcribed region of the human growth hormone gene. However, a previously described glucocorticoid receptor binding site in the first intron of the gene is not required for response to the hormone.

L56 ANSWER 28 OF 37 HCAPLUS COPYRIGHT 2001 ACS
AN 1986:547447 HCAPLUS
DN 105:147447
TI Human growth hormone as a reporter gene in regulation studies employing

transient gene expression
AU **Selden, Richard F.**; Howie, Kathleen Burke; Rowe, Mary Ellen; Goodman, Howard M.; Moore, David D.
CS Harvard Med. Sch., Massachusetts Gen. Hosp., Boston, MA, 02114, USA
SO Mol. Cell. Biol. (1986), 6(9), 3173-9
CODEN: MCEBD4; ISSN: 0270-7306
DT Journal
LA English
AB The human growth hormone (hGH) [12629-01-5] transient assay system is based on the expression of hGH directed by cells transfected with hGH fusion genes. Levels of secreted hGH in the medium, measured by a simple RIA, are proportional to both levels of cytoplasmic hGH **mRNA** and the amt. of transfected DNA. The system is extremely sensitive, easy to perform, and is qual. different from other transient expression systems in that the medium is assayed and the cells themselves are not destroyed. The hGH transient assay system is appropriate for analyses of regulation of gene expression and was used to examine the effect of the SV40 virus enhancer on the herpes simplex virus thymidine kinase [9002-06-6] promoter and the effect of Zn on the mouse metallothionein-I promoter. The expression of hGH can also be used as an internal control to monitor transfection efficiency along with any other transient expression system. All cell types tests thus far (including AtT-20, CV-1, GC, GH4, JEG, L, and primary pituitary cells) were able to secrete hGH into the medium.

L56 ANSWER 29 OF 37 HCAPLUS COPYRIGHT 2001 ACS
AN 1985:432910 HCAPLUS
DN 103:32910
TI Identification and comparison of two sequence elements that confer cell-type specific transcription in yeast
AU **Miller, Allan M.**; MacKay, Vivian L.; Nasmyth, Kim A.
CS Lab. Mol. Biol., MRC, Cambridge, MA, CB2 2QH, USA
SO Nature (London) (1985), 314(6012), 598-603
CODEN: NATUAS; ISSN: 0028-0836
DT Journal
LA English
AB DNA sequences were identified that are recognized by gene MAT.alpha.2 protein and gene MATa1 protein-gene MAT.alpha.2 protein repression systems of Saccharomyces cerevisiae. The a1/.alpha.2 control of the HO gene was shown to be redundant; .gtoreq.2 control sites exist in the region -1777 to -296. A 20-base-pair control-sequence motif for the a1/.alpha.2 system was found in genes MAT.alpha., STE5, and HO. A related, but distinct, sequence was found in genes repressed by the gene MAT.alpha.2 protein alone. When either of these control sequences were attached to the gene CYC1 promoter, gene CYC1 expression was brought under cell type-specific control.

L56 ANSWER 30 OF 37 HCAPLUS COPYRIGHT 2001 ACS
AN 1984:484810 HCAPLUS
DN 101:84810
TI The yeast MATa1 gene contains two introns
AU **Miller, A. M.**
CS Lab. Mol. Biol., Cambridge, CB2 2QH, UK
SO EMBO J. (1984), 3(5), 1061-5
CODEN: EMJODG; ISSN: 0261-4189
DT Journal
LA English
AB In Saccharomyces cerevisiae, there are 2 mating types, a and .alpha., which may mate to produce an a/.alpha. diploid. Mating type is detd. by the allele (MATa or MAT.alpha.) occupying the MAT locus. In a diploid, expression of the MATa1 and MAT.alpha.2 genes dets. the a/.alpha. state by regulating the expression of unlinked genes. Previous S1 endonuclease mapping implied that the MATa1 transcript is not processed. Further S1 mapping of this transcript showed that the MATa1 gene contains 2 introns, unlike any other characterized nuclear gene in yeast. Both introns contain 5' splice sites and 5'-TACTAACA-3' consensus sequences at the positions predicted by the S1 mapping data. In the splicing-defective

rna2 mutant, the mature message disappears rapidly, and the precursor RNA accumulates. The RNA processing removes the UGA stop **codon** which was previously believed to be read-though.

L56 ANSWER 31 OF 37 HCAPLUS COPYRIGHT 2001 ACS
AN 1984:62613 HCAPLUS
DN 100:62613
TI Transfer RNA genes of Zea mays chloroplast DNA
AU **Selden, Richard F.**; Steinmetz, Andre; McIntosh, Lee; Bogorad, Lawrence; Burkard, Gerard; Mubumbila, Mfika; Kuntz, Marcel; Crouse, Edwin J.; Weil, Jacques H.
CS Biol. Lab., Harvard Univ., Cambridge, MA, USA
SO Plant Mol. Biol. (1983), 2(3), 141-53
CODEN: PMBIDB; ISSN: 0167-4412
DT Journal
LA English
AB A min. of 37 genes, corresponding to tRNAs for 17 different amino acids, were localized on the restriction endonuclease cleavage site map of the Z. mays chloroplast DNA mol. Of these, 14 genes, corresponding to tRNAs for 11 amino acids, are located in the larger of the 2 single-copy regions which sep. the 2 inverted copies of the repeat region. One tRNA gene is in the smaller single-copy region. Each copy of the large repeated sequence contains, in addn. to the rRNA genes, 11 tRNA genes corresponding to tRNAs for 8 amino acids. The genes for tRNA2Ile and tRNAAla map in the ribosomal spacer sequence sepg. the 16 S and 23 S rRNA genes. The 3 isoaccepting species for the tRNAsLeu and the 3 for tRNAsSer, as well as the 2 isoaccepting species for tRNAAsn, tRNAGly, tRNAsIle, tRNAsMet, and tRNAsThr, are encoded at different loci. Two independent methods were used for the localization of tRNA genes on the phys. map of the maize chloroplast DNA mol.: (1) cloned chloroplast DNA fragments were hybridized with radioactively labeled total 4 S RNAs, and the hybridized RNAs were then eluted and identified by 2-dimensional polyacrylamide gel electrophoresis, and (2) individual tRNAs were 32P-labeled in vitro and hybridized to DNA fragments generated by digestion of maize chloroplast DNA with various restriction endonucleases.

L56 ANSWER 32 OF 37 HCAPLUS COPYRIGHT 2001 ACS
AN 1984:46090 HCAPLUS
DN 100:46090
TI Gene mapping studies and sequence determination of chloroplast tRNAs from various photosynthetic organisms
AU Weil, J. H.; Mubumbila, M.; Kuntz, M.; Keller, M.; Steinmetz, A.; Crouse, E. J.; Burkard, G.; Guillemaut, P.; **Selden, R.**; et al.
CS Inst. Mol. Cell. Biol., Natl. Cent. Sci. Res., Strasbourg, Fr.
SO Mol. Biol. (Moscow) (1983), 17(6), 1147-53
CODEN: MOBIBO; ISSN: 0026-8984
DT Journal; General Review
LA Russian
AB A review with 22 refs.

L56 ANSWER 33 OF 37 HCAPLUS COPYRIGHT 2001 ACS
AN 1984:30286 HCAPLUS
DN 100:30286
TI Comparative studies on tRNAs and aminoacyl-tRNA synthetases from various photosynthetic organisms
AU Weil, J. H.; Mubumbila, M.; Kuntz, M.; Keller, M.; Crouse, E. J.; Burkard, G.; Guillemaut, P.; **Selden, R.**; McIntosh, L.; et al.
CS IBMC, Strasbourg, Fr.
SO NATO Adv. Sci. Inst. Ser., Ser. A (1983), 63(Struct. Funct. Plant Genomes), 167-80
CODEN: NALSDJ
DT Journal; General Review
LA English
AB A review with 31 refs., with special emphasis on the mapping of tRNA genes on the chloroplast DNA of various photosynthetic organisms.

L56 ANSWER 34 OF 37 HCAPLUS COPYRIGHT 2001 ACS
AN 1983:138223 HCAPLUS
DN 98:138223
TI Gene mapping studies and sequence determination on chloroplast transfer RNAs from various photosynthetic organisms
AU Weil, J. H.; Mubumbila, M.; Kuntz, M.; Keller, M.; Steinmetz, A.; Crouse, E. J.; Burkard, G.; Guillemaut, P.; **Selden, R.**; et al.
CS IBMC, Strasbourg, Fr.
SO Prog. Clin. Biol. Res. (1982), 102(Cell Funct. Differ., Pt. B), 321-31
CODEN: PCBRD2; ISSN: 0361-7742
DT Journal; General Review
LA English
AB A review with 20 refs. on chloroplast tRNA genes and genetic map assignments in Zea mays, Phaseolus vulgaris, Euglena gracilis, and Cyanophora paradoxa.

L56 ANSWER 35 OF 37 HCAPLUS COPYRIGHT 2001 ACS
AN 1983:120438 HCAPLUS
DN 98:120438
TI The ribosomal gene nontranscribed spacer
AU **Treco, Douglas**; Brownell, Elise; Arnheim, Norman
CS Dep. Biochem., State Univ. New York, Stony Brook, NY, 11794, USA
SO Cell Nucl. (1982), Volume 12, Issue rDNA, Pt. C, 101-26. Editor(s): Busch, Harris; Rothblum, Lawrence. Publisher: Academic, New York, N. Y.
CODEN: 29DFAN
DT Conference; General Review
LA English
AB A review with 138 refs.

L56 ANSWER 36 OF 37 HCAPLUS COPYRIGHT 2001 ACS
AN 1982:521301 HCAPLUS
DN 97:121301
TI Distribution of ribosomal gene length variants among mouse chromosomes
AU Arnheim, Norman; **Treco, Douglas**; Taylor, Benjamin; Eicher, Eva M.
CS Biochem. Dep., State Univ. New York, Stony Brook, NY, 11794, USA
SO Proc. Natl. Acad. Sci. U. S. A. (1982), 79(15), 4677-80
CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English
AB The ribosomal genes (rDNA) in mouse inbred strains have a multichromosomal distribution. Using a structural feature of rDNA [variable length rDNA segment (VrDNA)] that shows length polymorphism within and among inbred strains, the chromosomal distribution of the variant ribosomal gene types were studied by genetic anal. Five of the length variant classes can be divided into 3 discrete linkage groups. The variants present on a particular chromosome pair appear to be unique to that pair and absent from nonhomologous chromosomes. The chromosomal location of particular variants appears to be the same in 2 unrelated inbred strains suggesting that the obsd. linkage patterns predate the origin of inbred mice. The nonrandom chromosomal distribution of these rDNA classes suggests that only a limited degree of genetic exchange occurs among nucleolus organizer regions on nonhomologous chromosomes. One particular VrDNA linkage group was localized to chromosome 12. These and other restriction fragment polymorphisms can be used in the construction of detailed mouse linkage maps.

L56 ANSWER 37 OF 37 HCAPLUS COPYRIGHT 2001 ACS
AN 1981:170727 HCAPLUS
DN 94:170727
TI An investigation of the structure of Alfalfa mosaic virus by small-angle neutron scattering
AU Cusack, S.; **Miller, A.**; Krijgsman, P. C. J.; Mellema, J. E.
CS EMBL Outstn., CEN, Grenoble, 38041, Fr.
SO J. Mol. Biol. (1981), 145(3), 525-43
CODEN: JMOBAK; ISSN: 0022-2836

DT Journal
LA English
AB Small-angle neutron scattering expts. performed on the tubular bottom component of alfalfa mosaic virus (AMV) and the 30 S particle (a quasispherical reassembled AMV coat protein particle) led to the construction of 3 models. A single homogeneous shell was inadequate, and of the 2 other models introducing the presumed T = 1 icosahedral symmetry of the particle, the most satisfactory consisted of 60 spherical monomers of radius 19 .ANG. sym. placed in pairs about the 2-fold icosahedral positions. Anal. of the bottom component data yielded a low-resoln. model for the virus, in which the RNA was uniformly packed throughout the interior of the capsid (which is cylindrical with hemispherical ends) out to a radius of .apprx.65 .ANG. and with a packing fraction of 20%. Within the limitations of a homogeneous shell model, the protein capsid had an outer radius of 94 .ANG. and a thickness of 23 .ANG.; but arguments are presented, based on the marked lattice structure of the cylindrical capsid and the anal. of the scattering data of the 30 S particle, that this model underests. the thickness of the protein shell, and that it makes contact with the RNA at .apprx.65 .ANG..

=> fil medline

FILE 'MEDLINE' ENTERED AT 13:55:49 ON 18 MAR 2001

FILE LAST UPDATED: 27 OCT 2000 (20001027/UP). FILE COVERS 1958 TO DATE.

MEDLINE now contains new records from the former NLM HEALTH STAR database. These records have an Entry Date and Update Date of 20010223.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2001 vocabulary. Enter HELP THESAURUS for details.

The OLDMEDLINE file segment now contains data from 1958 through 1965. Enter HELP CONTENT for details.

Left, right, and simultaneous left and right truncation are available in the Basic Index. See HELP SFIELDS for details.

THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE SUBSTANCE IDENTIFICATION.

MEDLINE UPDATES ARE ON HOLD UNTIL AFTER THE ANNUAL RELOAD HAS BEEN COMPLETED. NOTICE WILL BE GIVEN ONCE THE RELOAD IS COMPLETED AND RELOAD DETAILS WILL BE FOUND IN HELP RLOAD.

=> d his 157-

(FILE 'HCAPLUS' ENTERED AT 13:32:47 ON 18 MAR 2001)

FILE 'MEDLINE' ENTERED AT 13:33:18 ON 18 MAR 2001
L57 252047 S RNA+NT/CT
L58 95278 S L57/MAJ
L59 41410 S L58 AND RNA, MESSENGER+NT/CT
L60 87700 S L58 AND PY<=1998
L61 37303 S L59 AND L60
L62 50 S L61 AND GENES, SYNTHETIC+NT/CT
L63 1277 S L61 AND RECOMBINATION, GENETIC+NT/CT
L64 9336 S L61 AND GENE EXPRESSION REGULATION+NT/CT
L65 14554 S L61 AND BASE SEQUENCE+NT/CT
L66 401 S L61 AND BASE COMPOSITION+NT/CT
L67 2934 S L61 AND CODON+NT/CT
L68 628 S L61 AND INTRONS+NT/CT
L69 2919 S L61 AND G5.331.375.700./CT
L70 3505 S L61 AND GENETIC CODE+NT/CT

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L71          948 S L61 AND EXONS+NT/CT
L72          492 S L61 AND (OPTIMAL? OR OPTIMIZ?)
L73         3192 S L61 AND (STABIL? OR STABL?)
L74          276 S L72 AND L62-L71
L75         2131 S L73 AND L62-L71
L76           43 S L74 AND L75
L77       143314 S RNA, MESSENGER+NT/CT
L78           34 S L77/MAJ AND L76
L79           34 S L78 AND G5./CT
L80         6319 S L18
L81         9461 S  FACTOR VIII+NT/CT
L82         9463 S L80,L81
L83           14 S L77/MAJ AND L82
L84           57 S L77 AND G5./CT AND L82
L85           12 S L84 AND L62-L76
L86           92 S L79,L83-L85
L87            4 S L86 AND (GENETIC VECTORS+NT)/CT
L88          288 S DNA MUTATIONAL ANALYSIS+NT/CT AND L77/MAJ
L89            2 S L88 AND L82
L90           92 S L86,L87,L89
L91          226 S L88 AND L62-L76
L92        31873 S SEQUENCE ANALYSIS, DNA+NT/CT
L93          493 S SEQUENCE ANALYSIS, RNA+NT/CT
L94           53 S L93 AND L77/MAJ
L95          145 S L90,L94
L96          440 S L93 NOT L95
L97          501 S L77/MAJ AND (OPTIMAL? OR OPTIMIZ?)
L98           34 S L97 AND L79
L99            1 S L97 AND L82
L100          35 S L97 AND L86
L101           2 S L97 AND L87
L102           9 S L97 AND L88
L103          35 S L97 AND L90
L104           7 S L97 AND L91
L105          36 S L97 AND L95
L106          43 S L98-L105
L107          41 S L106 AND L60
L108           2 S L106 NOT L107

     FILE 'MEDLINE' ENTERED AT 13:55:49 ON 18 MAR 2001

=> d all tot l107


L107 ANSWER 1 OF 41  MEDLINE
AN   1998241642     MEDLINE
DN   98241642
TI   Stability determinants are localized to the 3'-untranslated
     region and 3'-coding region of the neurofilament light subunit mRNA using
     a tetracycline-inducible promoter.
AU   Canete-Soler R; Schwartz M L; Hua Y; Schlaepfer W W
CS   Division of Neuropathology, Department of Pathology and Laboratory
     Medicine, University of Pennsylvania School of Medicine, Philadelphia,
     Pennsylvania 19104, USA.. racansol@mail.med.upenn.edu
SO   JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 May 15) 273 (20) 12650-4.
     Journal code: HIV. ISSN: 0021-9258.
CY   United States
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   Priority Journals; Cancer Journals
EM   199808
EW   19980803
AB   The tetracycline-responsive expression system of Bujard was used to
     compare rates of decay of wild-type and mutant neurofilament (NF) light
     subunit (NF-L) mRNAs. Optimal conditions for activation and
     inactivation of the target transgene were determined using a luciferase
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reporter gene. Analyses of mRNA **stability** were thereupon conducted on cells that were doubly transfected with transactivator and inducible target genes and derived from pooled clones of transfected cells. Rates of mRNA decay were compared upon inactivation of the transgenes after high levels of mRNA had been induced. Deletion of the 445-nucleotide (nt) 3'-untranslated region (3'-UTR) (L/++(+)-) or 527 nt of the 3'-coding region (3'-CR) (L/++-+) increased the **stability** of NF-L mRNA compared with the full-length (L/++(++)) transcript in neuronal (N2a and P19 cells) and non-neuronal (L cells) lines. Deletion of both the 3'-UTR and 3'-CR (L/++--) led to a further **stabilization** of the transcript. A major **stability** determinant was then localized to a 68-nt sequence that forms the junction between the 3'-CR and 3'-UTR of NF-L and is the binding site of a unique ribonucleoprotein complex (Canete-Soler, R., Schwartz, M. L., Hua, Y., and Schlaepfer, W. W. (1998) J. Biol. Chem. 273, 12655-12661). The studies establish a novel system for mapping determinants of mRNA **stability** and have applied the system to localize determinants that regulate the **stability** of the NF-L mRNA.

CT Check Tags: Animal
Cell Line
Mice
*Neurofilament Proteins: GE, genetics
***Promoter Regions (Genetics)**
***RNA, Messenger: GE, genetics**
*Tetracycline: PD, pharmacology
*Trans-Activators: ME, metabolism
***Translation, Genetic**

RN 60-54-8 (Tetracycline)

CN 0 (neurofilament protein L); 0 (Neurofilament Proteins); 0 (RNA, Messenger); 0 (Trans-Activators)

L107 ANSWER 2 OF 41 MEDLINE

AN 97465800 MEDLINE

DN 97465800

TI Probing the structure of the regulatory region of human transferrin receptor messenger RNA and its interaction with iron regulatory protein-1.

AU Schlegl J; Gegout V; Schlager B; Hentze M W; Westhof E; Ehresmann C; Ehresmann B; Romby P

CS UPR 9002 du CNRS, Institut de Biologie Moleculaire et Cellulaire, Strasbourg, France.

SO RNA, **(1997 Oct)** 3 (10) 1159-72.
Journal code: CHB. ISSN: 1355-8382.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199801

EW 19980104

AB A portion of the 3'UTR of the human transferrin receptor mRNA mediates iron-dependent regulation of mRNA **stability**. The minimal RNA regulatory region contains three conserved hairpins, so-called iron responsive elements (IREs), that are recognized specifically by iron regulatory proteins (IRPs). The structure of this regulatory region and its complex with IRP-1 was probed using a combination of enzymes and chemicals. The data support the existence of an intrinsic IRE loop structure that is constrained by an internal C-G base pair. This particular structure is one of the determinants required for **optimal** IRP binding. IRP-1 covers one helical turn of the IRE and protects conserved residues in each of the three IREs: the bulged cytosine and nucleotides in the hairpin loops. Two essential IRP-phosphate contacts were identified by ethylation interference. Three-dimensional modeling of one IRE reveals that IRP-1 contacts several bases and the ribose-phosphate backbone located on one face in the deep groove, but contacts also exist with the shallow groove. A conformational change of the IRE loop mediated by IRP-1 binding was visualized by Pb2+-catalyzed hydrolysis. This effect is dependent on the loop structure and on the nature of the closing base

pair. Within the regulatory region of transferrin receptor mRNA, IRP-1 induces reactivity changes in a U-rich hairpin loop that requires the presence of the stem-loop structure located just downstream the endonucleolytic cleavage site identified by Binder et al. (Binder R et al. 1994, EMBO J 13:1969-1980). These results provide indications of the mechanism by which IRP-1 **stabilizes** the transferrin receptor mRNA under iron depletion conditions.

CT Check Tags: Human; Support, Non-U.S. Gov't
**Base Composition**
**Base Sequence**
Binding Sites
Electrophoresis, Polyacrylamide Gel
Ethylnitrosourea: PD, pharmacology
Hydrolysis
Hydroxyl Radical: ME, metabolism
Iron: ME, metabolism
*Iron-Sulfur Proteins: ME, metabolism
Lead: PD, pharmacology
Models, Molecular
**Molecular Sequence Data**
**Mutation**
*Nucleic Acid Conformation
*Receptors, Transferrin: GE, genetics
Ribonuclease T1: ME, metabolism
*RNA-Binding Proteins: ME, metabolism
***RNA, Messenger: CH, chemistry**
**RNA, Messenger: ME, metabolism**

RN 3352-57-6 (Hydroxyl Radical); 7439-89-6 (Iron); 7439-92-1 (Lead); 759-73-9 (Ethylnitrosourea)

CN EC 3.1.27.3 (Ribonuclease T1); 0 (iron regulatory factor); 0 (Iron-Sulfur Proteins); 0 (Receptors, Transferrin); 0 (RNA-Binding Proteins); 0 (RNA, Messenger)

L107 ANSWER 3 OF 41 MEDLINE
AN 97400260 MEDLINE
DN 97400260
TI An extracellular factor regulating expression of the chromosomal aminoglycoside 2'-N-acetyltransferase of Providencia stuartii.
AU Rather P N; Parojcic M M; Paradise M R
CS Department of Medicine, Case Western Reserve University School of Medicine, Veterans Affairs Medical Center, Cleveland, Ohio 44106, USA.. pxr17@po.cwru.edu
SO ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, **(1997 Aug)** 41 (8) 1749-54.
Journal code: 6HK. ISSN: 0066-4804.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199711
EW 19971104
AB The chromosomal aac(2')-Ia gene in Providencia stuartii encodes a housekeeping 2'-N-acetyltransferase [AAC(2')-Ia] involved in the acetylation of peptidoglycan. In addition, the AAC(2')-Ia enzyme also acetylates and confers resistance to the clinically important aminoglycoside antibiotics gentamicin, tobramycin, and netilmicin. Expression of the aac(2')-Ia gene was found to be strongly influenced by cell density, with a sharp decrease in aac(2')-Ia mRNA accumulation as cells approached stationary phase. This decrease was mediated by the accumulation of an extracellular factor, designated AR (for acetyltransferase repressing)-factor. AR-factor was produced in both minimal and rich media and acted in a manner that was strongly dose dependent. The activity of AR-factor was also pH dependent, with **optimal** activity at pH 8.0 and above. Biochemical characterization of conditioned media from P. stuartii has shown that AR-factor is between 500 and 1,000 Da in molecular size and is heat **stable**. In

addition, AR-factor was inactivated by a variety of proteases, suggesting that it may be a small peptide.
CT Check Tags: Support, U.S. Gov't, Non-P.H.S.
Acetyltransferases: AI, antagonists & inhibitors
*Acetyltransferases: GE, genetics
Acetyltransferases: ME, metabolism
***Gene Expression Regulation, Enzymologic**
***Genes, Bacterial**
*Providencia: EN, enzymology
Providencia: GE, genetics
*Repressor Proteins: ME, metabolism
***RNA, Messenger: ME, metabolism**
CN EC 2.3.1. (Acetyltransferases); EC 2.3.1.59 (gentamicin 2'-N-acetyltransferase); 0 (Repressor Proteins); 0 (RNA, Messenger)

L107 ANSWER 4 OF 41 MEDLINE
AN 97361802 MEDLINE
DN 97361802
TI mRNA **stability** is regulated by a coding-region element and the unique 5' untranslated leader sequences of the three Synechococcus psbA transcripts.
AU Kulkarni R D; Golden S S
CS Department of Biology, Texas A&M University, College Station 77843-3258, USA.
NC GM37040 (NIGMS)
SO MOLECULAR MICROBIOLOGY, **(1997 Jun)** 24 (6) 1131-42.
Journal code: MOM. ISSN: 0950-382X.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199711
AB The psbAI and psbAIII transcripts in Synechococcus sp. strain PCC 7942 are subject to accelerated turnover when cells are exposed to high light intensities, but psbAII message **stability** is unaffected. We used a psbAI 'minigene' which has a part of the coding sequence removed as a reporter gene in order to identify the cis-acting elements of the transcript that determine **stability**. While engineering the minigene to **optimally** mimic the native gene, we identified a **stabilizer** element within the open reading frame, corresponding to the coding region for the first membrane span of the D1 protein, the presence of and translation through which was essential for normal psbA mRNA **stability**. We propose that this **stabilizer** is a site for ribosome pausing, and that accumulation of ribosomes on the transcript upstream of the pause site increases **stability**. To identify the elements that regulate the differential responses of the psbA transcripts to high-light growth, sequences from psbAII and psbAIII were substituted in the psbAI minigene reporter. The chimeric reporter transcripts established that the psbAI and psbAIII untranslated leaders determine the faster turnover of these messages. The untranslated leader regions of the psbA transcripts may regulate mRNA **stability** by modulating translation and thereby **stability**, or by recruiting RNA-binding proteins that affect mRNA turnover more directly.
CT Check Tags: Support, U.S. Gov't, P.H.S.
**Genes, Bacterial**
*Photosynthetic Reaction Center, Bacterial: GE, genetics
*Photosynthetic Reaction Center, Plant: GE, genetics
Ribosomes: ME, metabolism
**RNA Processing, Post-Transcriptional**
***RNA, Bacterial: ME, metabolism**
***RNA, Messenger: ME, metabolism**
*Synechococcus Group: GE, genetics
**Translation, Genetic**
RN 125389-73-3 (D1 photosystem II protein)
CN 0 (Photosynthetic Reaction Center, Bacterial); 0 (Photosynthetic Reaction Center, Plant); 0 (RNA, Bacterial); 0 (RNA, Messenger)

L107 ANSWER 5 OF 41 MEDLINE
AN 97320958 MEDLINE
DN 97320958
TI Use of thermostable and Escherichia coli RNase H in RNA mapping studies.
AU Porter D; Curthoys N P
CS Department of Biochemistry and Molecular Biology, Colorado State University, Fort Collins 80523-1870, USA.
NC DK-37124 (NIDDK)
SO ANALYTICAL BIOCHEMISTRY, **(1997 May 1)** 247 (2) 279-86.
Journal code: 4NK. ISSN: 0003-2697..
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199709
EW 19970902
AB A recently introduced thermostable RNase H was tested to determine its effectiveness in RNase H mapping reactions. Procedures are described which should have general use with both the thermostable and the Escherichia coli RNase H enzymes. Using the thermostable RNase H at higher temperatures extends the range of oligodeoxyribonucleotide/RNA combinations that yield satisfactory results. Northern blot analyses of total RNA was used to demonstrate that native RNAs can be analyzed by oligodeoxyribonucleotide directed RNase H digestion with minimal sample processing as long as care is taken to maintain thermal stringency both during reaction assembly and termination. Increased thermal stringency allows for higher DNA concentrations to ensure complete site-specific digestion of target RNAs or to permit simultaneous cleavage with multiple oligodeoxyribonucleotides. Partial digests can also be controlled by manipulating oligodeoxyribonucleotide concentrations. In addition, the thermostable RNase H was shown to be active at magnesium ion concentrations as low as 0.1 mM. This allows for **optimization** of Mg2+ effects on overall sample integrity and DNA/RNA interactions over at least a 20-fold range (2.0-0.1 mM).
CT Check Tags: Animal; Support, U.S. Gov't, P.H.S.
**Base Sequence**
Binding Sites
DNA, Complementary: GE, genetics
**Enzyme Stability**
Escherichia coli: EN, enzymology
Oligodeoxyribonucleotides: GE, genetics
Rats
*Ribonuclease H, Calf Thymus
***RNA, Messenger: GE, genetics**
***RNA, Messenger: IP, isolation & purification**
Swine
Temperature
CN EC 3.1.26.4 (Ribonuclease H, Calf Thymus); 0 (DNA, Complementary); 0 (Oligodeoxyribonucleotides); 0 (RNA, Messenger)

L107 ANSWER 6 OF 41 MEDLINE
AN 97301058 MEDLINE
DN 97301058
TI Does Escherichia coli **optimize** the economics of the translation process?.
AU Solomovici J; Lesnik T; Reiss C
CS Centre de Genetique Moleculaire, CNRS, Gif Sur Yvette, France.
SO JOURNAL OF THEORETICAL BIOLOGY, **(1997 Apr 21)** 185 (4) 511-21.
Journal code: K8N. ISSN: 0022-5193.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199708
EW 19970804

AB The codon translation rate is usually assumed to be proportional to the cellular concentration of the cognate tRNA, but synonymous codons sharing the same cognate tRNA may be translated at rather different rates. To account for the latter observation, we assume that the translation process is **optimized** in two respects: (i), the codon demand is **optimized** with respect to the supply of cognate tRNAs (composition of the tRNA pool); and (ii), for synonymous codons sharing the same cognate tRNA, the usage frequency of each codon correlates **optimally** with the **stability** of the codon-anticodon complex. These assumptions allow us to compute the relative rate constants of synonymous codons. Highly expressed genes, which produce 80-90% of the protein mass in the E. coli cell, appear to have selected codons which make an **optimal** use of the tRNA pool. Assuming the **optimization** criteria were valid, a list of codon translation times (in ms) were derived from available experimental data.

CT ***Codon, Terminator**
*Escherichia coli: GE, genetics
***Genes, Bacterial**
***Models, Genetic**
***Translation, Genetic**

CN 0 (Codon, Terminator)

L107 ANSWER 7 OF 41 MEDLINE
AN 97153094 MEDLINE
DN 97153094
TI Efficient hammerhead ribozymes targeted to the polycistronic Sendai virus P/C mRNA. Structure-function relationships.
AU Gavin D K; Gupta K C
CS Department of Immunology/Microbiology, Rush Medical College, Chicago, Illinois 60612, USA.
NC AI30517 (NIAID)
SO JOURNAL OF BIOLOGICAL CHEMISTRY, **(1997 Jan 17)** 272 (3) 1461-72.
Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199704
EW 19970403
AB The Sendai virus polycistronic P/C mRNA encodes the P and C proteins from alternate overlapping reading frames. To determine the functions of these proteins in virus replication, hammerhead ribozymes were targeted to cleave the 5'-untranslated region of the P/C mRNA. Both cell-free and intracellular assays were employed to determine ribozyme efficacy. To appropriately compare activities between cell-free and intracellular assays, identical ribozymes were synthesized in vitro as well as expressed in cells. Ribozyme parameters, namely hybridization arm length (HAL) and nonhybridizing extraneous sequences (NES), were found to have rate-determining properties. In cell-free reactions, ribozymes with 13-mer HAL were up to 10-fold more efficient than those with 9-mer HAL. Ribozymes with 9-mer HAL were relatively ineffective in transfected cells. Minimizing the number of NES increased ribozyme efficiency in vitro. However, ribozymes with minimal NES were essentially inert intracellularly. The NES at the termini of the most effective intracellular ribozyme, Rz13st ( approximately 95% inhibition of the p gene expression), were predicted to fold into stem-loop structures. These structures most likely increase ribozyme **stability** as evidenced by the 8-fold higher resistance to ribonuclease T2 digestion of Rz13st compared with Rz13B. Our results suggest that when designing effective intracellular ribozymes, parameters that enhance formation of productive ribozyme:substrate duplexes and that increase RNA **stability** should be **optimized**.
CT Check Tags: Support, U.S. Gov't, P.H.S.
**Base Sequence**
Cell-Free System
**Molecular Sequence Data**

Oligodeoxyribonucleotides
*Paramyxovirus: GE, genetics
Protein Conformation
**RNA, Catalytic: CH, chemistry**
***RNA, Catalytic: ME, metabolism**
***RNA, Messenger: ME, metabolism**
***RNA, Viral: ME, metabolism**
Substrate Specificity
CN 0 (Oligodeoxyribonucleotides); 0 (RNA, Catalytic); 0 (RNA, Messenger); 0 (RNA, Viral)

L107 ANSWER 8 OF 41 MEDLINE
AN 96332659 MEDLINE
DN 96332659
TI mRNA sequences influencing translation and the selection of AUG initiator codons in the yeast Saccharomyces cerevisiae.
AU Yun D F; Laz T M; Clements J M; Sherman F
CS Department of Biochemistry, University of Rochester, School of Medicine and Dentistry, New York 14642, USA.
NC T32 GM07098 (NIGMS)
R01 GM12702 (NIGMS)
SO MOLECULAR MICROBIOLOGY, **(1996 Mar)** 19 (6) 1225-39.
Journal code: MOM. ISSN: 0950-382X.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199611
AB The secondary structure and sequences influencing the expression and selection of the AUG initiator codon in the yeast Saccharomyces cerevisiae were investigated with two fused genes, which were composed of either the CYC7 or CYC1 leader regions, respectively, linked to the lacZ coding region. In addition, the strains contained the upf1-delta disruption, which **stabilized** mRNAs that had premature termination codons, resulting in wild-type levels. The following major conclusions were reached by measuring beta-galactosidase activities in yeast strains having integrated single copies of the fused genes with various alterations in the 89 and 38 nucleotide-long untranslated CYC7 and CYC1 leader regions, respectively. The leader region adjacent to the AUG initiator codon was dispensable, but the nucleotide preceding the AUG initiator at position -3 modified the efficiency of translation by less than twofold, exhibiting an order of preference A > G > C > U. Upstream out-of-frame AUG triplets diminished initiation at the normal site, from essentially complete inhibition to approximately 50% inhibition, depending on the position of the upstream AUG triplet and on the context (-3 position nucleotides) of the two AUG triplets. In this regard, complete inhibition occurred when the upstream and downstream AUG triplets were closer together, and when the upstream and downstream AUG triplets had, respectively, **optimal** and suboptimal contexts. Thus, leaky scanning occurs in yeast, similar to its occurrence in higher eukaryotes. In contrast, termination codons between two AUG triplets causes reinitiation at the downstream AUG in higher eukaryotes, but not generally in yeast. Our results and the results of others with GCN4 mRNA and its derivatives indicate that reinitiation is not a general phenomenon in yeast, and that special sequences are required.
CT Check Tags: Support, U.S. Gov't, P.H.S.
**Base Sequence**
***Codon, Initiator: GE, genetics**
DNA, Fungal: GE, genetics
**Genes, Fungal**
**Genetic Vectors**
**Molecular Sequence Data**
Nucleic Acid Conformation
Plasmids: GE, genetics
**RNA, Fungal: CH, chemistry**
***RNA, Fungal: GE, genetics**

**RNA, Messenger: CH, chemistry**
***RNA, Messenger: GE, genetics**
*Saccharomyces cerevisiae: GE, genetics
**Translation, Genetic**
CN 0 (Codon, Initiator); 0 (DNA, Fungal); 0 (Genetic Vectors); 0 (Plasmids); 0 (RNA, Fungal); 0 (RNA, Messenger)

L107 ANSWER 9 OF 41 MEDLINE
AN 96235223 MEDLINE
DN 96235223
TI The synthesis of mRNA in isolated mitochondria can be maintained for several hours and is inhibited by high levels of ATP.
AU Enriquez J A; Fernandez-Silva P; Perez-Martos A; Lopez-Perez M J; Montoya J
CS Departamento de Bioquimica y Biologia Molecular y Celular, Universidad de Zaragoza, Spain.
SO EUROPEAN JOURNAL OF BIOCHEMISTRY, **(1996 May 1)** 237 (3) 601-10. Journal code: EMZ. ISSN: 0014-2956.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199609
AB The dependence for the maintenance of the synthesis and maturation of mitochondrial RNA on the supply of nucleo-cytoplasmic factors has been investigated by a novel in organello RNA synthesis system. We found that mitochondrial DNA transcription can be maintained for several hours in isolated mitochondria. Analysis of the individual mitochondrial RNA species revealed that: the processing of the rRNA precursors and the **stability** of the mature rRNAs, but not the transcription itself, is severely impaired after short periods of incubation, indicating that these processes are strongly dependent on the mitochondrial interaction with the nucleo-cytoplasmic compartment; the events that lead to the synthesis, processing and turnover of the mitochondrial mRNAs do not require the continuous supply of nucleo-cytoplasmic factors, that are accumulated in excess by mitochondria. Furthermore, we present evidence indicating an inhibition of high ATP levels on the mitochondrial RNA polymerase activity, both in organello and in vitro. Consequently, it is proposed that mitochondrial mRNA synthesis can be regulated in response to changes in intramitochondrial ATP levels. This regulation of mitochondrial mRNA synthesis together with their very rapid turnover described here and elsewhere [Gelfand, R. & Attardi, G. (1981) Mol. Cell Biol. 1, 497-511], could represent a mechanism that would allow each individual mitochondrion to adjust its **optimal** levels of mRNA, and hence its translation capacity, in response to local energetic demands.
CT Check Tags: Animal; In Vitro; Male; Support, Non-U.S. Gov't
*Adenosine Triphosphate: ME, metabolism
Adenosine Triphosphate: PD, pharmacology
DNA-Directed RNA Polymerase: AI, antagonists & inhibitors
Energy Metabolism
Half-Life
Kinetics
Mitochondria, Liver: DE, drug effects
*Mitochondria, Liver: ME, metabolism
Rats
Rats, Wistar
**RNA Processing, Post-Transcriptional**
***RNA, Messenger: BI, biosynthesis**
**RNA, Messenger: GE, genetics**
**RNA, Messenger: ME, metabolism**
**RNA, Ribosomal: BI, biosynthesis**
**Transcription, Genetic**
RN 56-65-5 (Adenosine Triphosphate)
CN EC 2.7.7.6 (DNA-Directed RNA Polymerase); 0 (RNA, Messenger); 0 (RNA, Ribosomal)

L107 ANSWER 10 OF 41 MEDLINE
AN 96226185 MEDLINE
DN 96226185
TI The histone 3'-terminal stem-loop is necessary for translation in Chinese hamster ovary cells.
AU Gallie D R; Lewis N J; Marzluff W F
CS Department of Biochemistry, University of California, Riverside, CA 92521-0129, USA.
NC GM 29832 (NIGMS)
T32CA09156 (NCI)
SO NUCLEIC ACIDS RESEARCH, **(1996 May 15)** 24 (10) 1954-62.
Journal code: O8L. ISSN: 0305-1048.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199610
AB The metazoan cell cycle-regulated histone mRNAs are the only known cellular mRNAs that do not terminate in a poly(A) tall. Instead, mammalian histone mRNAs terminate in a highly conserved stem-loop structure which is required for 3'-end processing and regulates mRNA **stability**. The poly(A) tail not only regulates translational efficiency and mRNA **stability** but is required for the function of the cap in translation (m(7)GpppN). We show that the histone terminal stem-loop is functionally similar to a poly(A) tail in that it enhances translational efficiency and is co-dependent on a cap in order to establish an efficient level of translation. The histone stem-loop is sufficient and necessary to increase the translation of reporter mRNA in transfected Chinese hamster ovary cells but must be positioned at the 3'-terminus in order to function **optimally**. Mutations within the conserved stem or loop regions reduced its ability to facilitate translation. All histone mRNAs in higher plants are polyadenylated. The histone stem-loop did not function to influence translational efficiency or mRNA **stability** in plant protoplasts. These data demonstrate that the histone stem/loop directs efficient translation and that it is functionally analogous to a poly(A) tail.
CT Check Tags: Animal; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.
**Base Sequence**
*CHO Cells: ME, metabolism
**Drug Stability**
**Gene Expression Regulation**
**Genes, Reporter**
Hamsters
*Histones: GE, genetics
Luciferase: GE, genetics
**Molecular Sequence Data**
**Mutation**
Nucleic Acid Conformation
Poly A: CH, chemistry
Poly A: ME, metabolism
Reticulocytes: ME, metabolism
***RNA, Messenger: CH, chemistry**
**RNA, Messenger: ME, metabolism**
Structure-Activity Relationship
**Transfection**
***Translation, Genetic**
RN 24937-83-5 (Poly A)
CN EC 1.13.12.- (Luciferase); 0 (Histones); 0 (RNA, Messenger)

L107 ANSWER 11 OF 41 MEDLINE
AN 96105379 MEDLINE
DN 96105379
TI Kinetics of translation of gamma B crystallin and its circularly permutated variant in an in vitro cell-free system: possible relations to codon distribution and protein folding.

AU Komar A A; Jaenicke R
CS Institut fur Biophysik und Physikalische Biochemie, Universitat Regensburg, Germany.
SO FEBS LETTERS, **(1995 Dec 4)** 376 (3) 195-8.
Journal code: EUH. ISSN: 0014-5793.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199603
AB Analysis of nascent gamma B-crystallin peptides accumulating during in vitro translation in a rabbit reticulocyte lysate cell-free system was carried out. As a consequence of the irregular distribution of rare codons along the polypeptide chain of gamma B-crystallin, translation of the two-domain protein is a non-uniform process characterized by specific pauses. One of the major delays occurs during the translation of the connecting peptide between the domains. Comparing the kinetics of translation of natural gamma B-crystallin and its circularly permutated variant (with the order of the N- and C-terminal domains exchanged) reveals that the natural N-terminal domain is translated faster than the C-terminal one. Since the N-terminal domain in natural gamma B-crystallin is known to be more **stable** and to fold faster than the C-terminal one [E.-M. Mayr et al. (1994) J. Mol. Biol. 235, 84-88], the present data suggest that the translation rates are **optimized** to tune the synthesis and folding of the nascent polypeptide chain. In this connection, the pause in the linker region between the domains provides a delay allowing the correct folding of the N-terminal domain and its subsequent assistance in the **stabilization** of the C-terminal one.
CT Check Tags: Animal; Support, Non-U.S. Gov't
Cattle
Cell-Free System
***Codon**
*Crystallins: CH, chemistry
Crystallins: GE, genetics
Kinetics
Protein Folding
Rabbits
Reticulocytes
**RNA, Messenger: GE, genetics**
***Translation, Genetic**
CN 0 (Codon); 0 (Crystallins); 0 (RNA, Messenger)

L107 ANSWER 12 OF 41 MEDLINE
AN 96104564 MEDLINE
DN 96104564
TI Translational efficiency is regulated by the length of the 3' untranslated region.
AU Tanguay R L; Gallie D R
CS Department of Biochemistry, University of California, Riverside 92521-0129, USA.
SO MOLECULAR AND CELLULAR BIOLOGY, **(1996 Jan)** 16 (1) 146-56.
Journal code: NGY. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199603
AB All polyadenylated mRNAs contain sequence of variable length between the coding region and the poly(A) tail. Little has been done to establish what role the length of the 3' untranslated region (3'UTR) plays in posttranscriptional regulation. Using firefly luciferase (luc) reporter mRNA in transiently transfected Chinese hamster ovary (CHO) cells, we observed that the addition of a poly(A) tail increased expression 97-fold when the length of the 3'UTR was 19 bases but that its stimulatory effect was only 2.3-fold when the length of the 3'UTR was increased to 156 bases.

The effect of the luc 3'UTR on poly(A) tail function was orientation independent, suggesting that its length and not its primary sequence was the important factor. Increasing the length of the 3'UTR increased expression from poly(A)- mRNA but had little effect on poly(A)+ mRNA. To examine the effect of length on translational efficiency and mRNA **stability**, a 20-base sequence was introduced and reiterated downstream of the luc stop codon to generate a nested set of constructs in which the length of the 3'UTR increased from 4 to 104 bases. For poly(A)- reporter mRNA, translational efficiency in CHO cells increased 38-fold as the length of the 3'UTR increased from 4 to 104 bases. Increasing the length of the 3'UTR beyond 104 bases increased expression even further. Increasing the length of the 3'UTR also resulted in a 2.5-fold **stabilization** of the reporter mRNA. For poly(A)+ mRNA, the translational efficiency and mRNA half-life increased only marginally as the length of the 3'UTR increased from 27 to 161 bases. However, positioning the poly(A) tail only 7 bases downstream of the stop codon resulted in a 39-fold reduction in the rate of translation relative to a construct with a 27-base 3'UTR, which may be a consequence of the poly(A) tail-poly(A)-binding protein complex functioning as a steric block to translocating ribosomes as they approached the termination codon. The **optimal** length of the 3' noncoding region for maximal poly(A) tail-mediated stimulation of translation is approximately 27 bases. These data suggest that the length of the 3'UTR plays an important role in determining both the translational efficiency and the **stability** of an mRNA.

CT Check Tags: Animal; Support, U.S. Gov't, Non-P.H.S.
**Base Sequence**
CHO Cells
**Gene Expression**
Hamsters
Luciferase: GE, genetics
**Molecular Sequence Data**
Ribosomes: ME, metabolism
**RNA Caps: GE, genetics**
**RNA Caps: ME, metabolism**
**RNA Processing, Post-Transcriptional**
***RNA, Messenger: GE, genetics**
**RNA, Messenger: ME, metabolism**
**Transfection**
***Translation, Genetic**
CN EC 1.13.12.- (Luciferase); 0 (RNA Caps); 0 (RNA, Messenger)

L107 ANSWER 13 OF 41 MEDLINE
AN 96064307 MEDLINE
DN 96064307
TI Alternatively spliced human type 1 angiotensin II receptor mRNAs are translated at different efficiencies and encode two receptor isoforms.
AU Curnow K M; Pascoe L; Davies E; White P C; Corvol P; Clauser E
CS Institute National de la Sante et de la Recherche Medicale U36, Chaire de Medicine Experimentale Coll`ege de France, Paris.
NC DK-42169 (NIDDK)
SO MOLECULAR ENDOCRINOLOGY, **(1995 Sep)** 9 (9) 1250-62.
Journal code: NGZ. ISSN: 0888-8809.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-S80189; GENBANK-S80190; GENBANK-S80192; GENBANK-S80194; GENBANK-S80239
EM 199603
AB The peptide hormone angiotensin II (AngII) plays a principal role in regulating blood pressure and fluid homeostasis. Most of its known effects are mediated by a guanine nucleotide-regulatory protein (G protein)-coupled receptor pharmacologically defined as the type-1 AngII receptor or AT1. Characterization of cDNA and genomic clones shows that the human AT1 gene contains five exons and encodes two receptor isoforms

as a result of alternative splicing. Exon 5 contains the previously characterized open reading frame for AT1, and exons 1 to 3 are alternatively spliced upstream of it to generate several mRNA species, while transcripts containing exon 4 are of minor abundance. In an in vitro translation system, the presence of exon 1 was found to be extremely inhibitory to translation, probably because it can form a **stable** secondary structure at the RNA level. The alternatively spliced second exon also had a strong inhibitory effect on translation, presumably because it contains a minicistron commencing with an ATG in an **optimal** context for translation initiation. Exon 2 was similarly inhibitory to protein production in transfected cells, but exon 1 was found to enhance protein synthesis in this system. Transcripts containing exon 3 and 5, which comprise up to one-third of AT1 mRNAs in all tissues examined, encode a receptor with an amino-terminal extension of 32-35 amino acids. These transcripts were translated into a larger receptor isoform in vitro and produced a functional receptor with normal ligand binding and signaling properties in transfected cells.

CT Check Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
***Alternative Splicing**
**Amino Acid Sequence**
Bacteriophage lambda: GE, genetics
**Base Sequence**
Binding Sites
DNA, Complementary: CH, chemistry
**Exons**
**Molecular Sequence Data**
Nucleic Acid Conformation
**Open Reading Frames**
*Receptors, Angiotensin: GE, genetics
**RNA, Messenger: AN, analysis**
**RNA, Messenger: CH, chemistry**
***RNA, Messenger: GE, genetics**
Tissue Distribution
**Transcription, Genetic**
**Transfection**
***Translation, Genetic**
CN 0 (DNA, Complementary); 0 (Receptors, Angiotensin); 0 (RNA, Messenger)

L107 ANSWER 14 OF 41 MEDLINE
AN 96030185 MEDLINE
DN 96030185
TI [Use of thermostable DNA polymerase from Thermus thermophilus KTP in a combined reverse transcription and amplification reaction for detecting CD4 receptor mRNA].
Ispol'zovanie termostabil'noi DNK-polimerazy iz Thermus thermophilus KTP v sovmeshchennoi reaktsii obratnoi transkriptsii i amplifikatsii dlia detektsii mRNK retseptora CD-4.
AU Glukhov A I; Grebennikova T V; Kiselev V I; Severin E S
SO MOLEKULIARNAIA BIOLOGIIA, **(1995 Jul-Aug)** 29 (4) 942-9.
Journal code: NGX. ISSN: 0026-8984.
CY RUSSIA: Russian Federation
DT Journal; Article; (JOURNAL ARTICLE)
LA Russian
FS Priority Journals
EM 199602
AB The RT/PCR method was applied to study a possible use of Tth DNA-polymerase for coupled reaction of reverse transcription and polymerase chain reaction (RT/PCR) on the CD-4 receptor mRNA template in the total cellular RNA. The conditions for detecting the CD-4 receptor mRNA were **optimized**. The pH-optimum for RT reaction was 8.8. The influence of Mn2+, Cu2+, Co2+, and Cd2+ cations in RT and PCR reaction was investigated. The efficiency of the RT reaction was shown to be the highest in the presence of Mn2+ (**optimal** concentration 1 mM). At Mn2+ concentration > or = 3 mM complete inhibition of RT/PCR was observed. The Tth DNA polymerase in RT/PCR was shown to be more effective than Taq DNA polymerase. The Tth DNA polymerase allows observation of the specific

product in the gel containing ethidium bromide using 20 ng of the total RNA. High sensitivity and specificity of RT/PCR performed with the Tth DNA polymerase allow its wide application in the detection, quantitative analysis and cloning of cellular and viral RNAs.

CT Check Tags: Human
***Antigens, CD4: GE, genetics**
**Base Sequence**
Cations, Divalent
Cell Line
DNA Primers
*DNA-Directed DNA Polymerase: ME, metabolism
English Abstract
**Enzyme Stability**
***Gene Amplification**
**Molecular Sequence Data**
Polymerase Chain Reaction
***RNA, Messenger: ME, metabolism**
*Thermus thermophilus: EN, enzymology
***Transcription, Genetic**
CN EC 2.7.7.7 (DNA-Directed DNA Polymerase); 0 (Antigens, CD4); 0 (Cations, Divalent); 0 (DNA Primers); 0 (RNA, Messenger)

L107 ANSWER 15 OF 41 MEDLINE
AN 95334381 MEDLINE
DN 95334381
TI Improved accumulation and activity of ribozymes expressed from a tRNA-based RNA polymerase III promoter.
AU Thompson J D; Ayers D F; Malmstrom T A; McKenzie T L; Ganousis L; Chowrira B M; Couture L; Stinchcomb D T
CS Ribozyme Pharmaceuticals Inc., Boulder, CO 80301, USA..
NC AI25959 (NIAID)
SO NUCLEIC ACIDS RESEARCH, **(1995 Jun 25)** 23 (12) 2259-68.
Journal code: O8L. ISSN: 0305-1048.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199510
AB RNA polymerase III (pol III) transcripts are abundant in all cells. Therefore, pol III promoters may be ideal for expressing high levels of exogenous RNAs, such as antisense RNAs, decoy RNAs and ribozymes, in many different cell types. We have improved accumulation of recombinant RNAs expressed from a human meti tRNA-derived pol III promoter > 100-fold by modifying the 3' terminus of the transcripts to hybridize to the 5' terminus. This terminal duplex includes the 8 nt leader sequence present in the primary wild-type meti tRNA transcript that is normally removed during processing to the mature tRNA. Expression of an anti-HIV ribozyme was analyzed in cells **stably** transduced with retroviral vectors encoding pol III transcription units containing this modification. High accumulation of recombinant pol III ribozyme transcripts was observed in all cell lines tested. Due to the enhanced transcript accumulation, ribozyme cleavage activity was readily detectable in total RNA extracted from **stably** transduced human T cell lines. One pol III transcription unit, termed 'TRZ', was **optimized** further for ribozyme cleavage activity. The improved pol III transcription units reported here may be useful for expressing a variety of functional and therapeutic RNAs.
CT Check Tags: Human; Support, U.S. Gov't, P.H.S.
**Base Sequence**
Blotting, Northern
Cell Line
**Gene Expression**
**Molecular Sequence Data**
Nucleic Acid Conformation
Plasmids
***Promoter Regions (Genetics)**

Retroviridae: GE, genetics
*RNA Polymerase III: GE, genetics
RNA Probes
**RNA, Catalytic: GE, genetics**
***RNA, Catalytic: ME, metabolism**
**RNA, Messenger: CH, chemistry**
***RNA, Messenger: ME, metabolism**
***RNA, Transfer, Met: GE, genetics**
CN EC 2.7.7.- (RNA Polymerase III); 0 (Plasmids); 0 (RNA Probes); 0 (RNA, Catalytic); 0 (RNA, Messenger); 0 (RNA, Transfer, Met)

L107 ANSWER 16 OF 41 MEDLINE
AN 95329733 MEDLINE
DN 95329733
TI **Optimization** of antisense oligodeoxynucleotide structure for targeting bcr-abl mRNA.
AU Giles R V; Spiller D G; Green J A; Clark R E; Tidd D M
CS Department of Biochemistry, University of Liverpool, UK.
SO BLOOD, **(1995 Jul 15)** 86 (2) 744-54.
Journal code: A8G. ISSN: 0006-4971.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199510
AB Antisense oligodeoxynucleotides targeted to bcr-abl are potential ex vivo purging agents for use with autologous bone marrow transplantation in the treatment of chronic myeloid leukemia (CML). We investigated, in a cell-free system, the activity and nuclease resistance of phosphodiester, phosphorothioate, chimeric methylphosphonate/phosphodiester, and chimeric methylphosphonate/phosphorothioate antisense octadecamers directed against either b2a2 or b3a2 bcr-abl breakpoint RNAs. Certain chimeric compounds were shown to possess targeted activity broadly equal to the parent phosphodiester or phosphorothioate forms and greater resistance to the nucleases present in cell extracts. Selected chimeric structures were compared with phosphodiester and phosphorothioate analogues for antisense activity in human CML cells containing either b2a2 or b3a2 bcr-abl breakpoint mRNAs. We present results showing that all four structures can suppress bcr-abl mRNA level in vivo. The rank of in vivo activity is chimeric methylphosphonate/phosphodiester > or = phosphodiester > phosphorothioate > methylphosphonate/phosphorothioate. We show that b2a2 breakpoint RNAs can be more effectively targeted than b3a2 sequence RNAs both in vitro and in vivo and suggest that RNA secondary structure may be a possible explanation for this phenomenon.
CT Check Tags: Human; Support, Non-U.S. Gov't
**Base Sequence**
Cell-Free System
Chromatography, High Pressure Liquid
**Drug Stability**
Endodeoxyribonucleases: ME, metabolism
*Fusion Proteins, bcr-abl: GE, genetics
***Gene Expression Regulation, Leukemic: DE, drug effects**
Leukemia, Lymphocytic, Acute: PA, pathology
**Molecular Sequence Data**
Nucleic Acid Conformation
*Oligonucleotides, Antisense: CH, chemistry
Oligonucleotides, Antisense: GE, genetics
Oligonucleotides, Antisense: PD, pharmacology
*Organophosphorus Compounds: PD, pharmacology
Polymerase Chain Reaction
***RNA, Messenger: AI, antagonists & inhibitors**
**RNA, Messenger: GE, genetics**
***RNA, Neoplasm: AI, antagonists & inhibitors**
**RNA, Neoplasm: GE, genetics**
*Thionucleotides: PD, pharmacology
Tumor Cells, Cultured

RN 993-13-5 (methylphosphonate)
CN EC 3.1.- (Endodeoxyribonucleases); 0 (Fusion Proteins, bcr-abl); 0 (Oligonucleotides, Antisense); 0 (Organophosphorus Compounds); 0 (RNA, Messenger); 0 (RNA, Neoplasm); 0 (Thionucleotides)
GEN bcr-abl; bcr

L107 ANSWER 17 OF 41 MEDLINE
AN 95303626 MEDLINE
DN 95303626
TI Defining a novel cis element in the 3'-untranslated region of mammalian ribonucleotide reductase component R2 mRNA: role in transforming growth factor-beta 1 induced mRNA **stabilization**.
AU Amara F M; Chen F Y; Wright J A
CS Manitoba Institute of Cell Biology, University of Manitoba, Winnipeg, Canada..
SO NUCLEIC ACIDS RESEARCH, **(1995 May 11)** 23 (9) 1461-7.
Journal code: O8L. ISSN: 0305-1048.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199509
AB Ribonucleotide reductase R2 gene expression is elevated in BALB/c 3T3 fibroblasts treated with transforming growth factor beta 1. We investigated the possibility that the 3'-UTR of ribonucleotide reductase R2 mRNA contains regulatory information for TGF-beta 1 induced message **stability**. Using end-labeled RNA fragments in gel shift assays and UV cross-linking analyses, we detected in the 3'-UTR a novel 9 nucleotide (nt) cis element, 5'-GAGUUUGAG-3' site, which interacted specifically with a cytosolic protease sensitive factor to form a 75 kDa complex. The cis element protein binding activity was inducible and markedly up-regulated cross-link 4 h after TGF-beta 1 treatment of mouse BALB/c 3T3 cells. Other 3'-UTRs [IRE, GM-CSF, c-myc and homopolymer (U)] were poor competitors to the cis element with regard to forming the TGF-beta 1 dependent RNA-protein complex. However, the cis element effectively competed out the formation of the R2 3'-UTR protein complex. Cytosolic extracts from a variety of mammalian cell lines (monkey Cos7, several mouse fibrosarcomas and human HeLa S3) demonstrated similar TGF-beta 1 dependent RNA-protein band shifts as cell extract from BALB/c 3T3 mouse fibroblasts. Binding was completely prevented by several different mutations within the cis element, and by substitution mutagenesis, we were able to predict the consensus sequences, 5'-GAGUUUNNN-3' and 5'-NNNUUUGAG-3' for **optimal** protein binding. These results support a model in which the 9 nt region functions in cis to destabilize R2 mRNA in cells; and upon activation, a TGF-beta 1 responsive protein is induced and interacts with the 9 nt cis element in a mechanism that leads to **stabilization** of the mRNA. This appears to be the first example of a mRNA binding site that is involved in TGF-beta 1-mediated effects.
CT Check Tags: Animal; Support, Non-U.S. Gov't
**Base Sequence**
Binding Sites: GE, genetics
Mice
Mice, Inbred BALB C
**Molecular Sequence Data**
**Mutation**
Protein Binding: GE, genetics
*Ribonucleotide Reductases: GE, genetics
***RNA, Messenger: GE, genetics**
**RNA, Messenger: ME, metabolism**
Sequence Analysis
*Transforming Growth Factor beta: ME, metabolism
Transforming Growth Factor beta: PD, pharmacology
3T3 Cells
CN EC 1.17.4 (Ribonucleotide Reductases); 0 (RNA, Messenger); 0 (Transforming Growth Factor beta)
GEN R2

L107 ANSWER 18 OF 41 MEDLINE
AN 95065647 MEDLINE
DN 95065647
TI Mutational analysis of the translational signal in the human cytomegalovirus gpUL4 (gp48) transcript leader by retroviral infection.
AU Cao J; Geballe A P
CS Department of Molecular Medicine, Fred Hutchinson Cancer Research Center, Seattle, Washington 98104.
NC AI26672 (NIAID)
SO VIROLOGY, **(1994 Nov 15)** 205 (1) 151-60.
Journal code: XEA. ISSN: 0042-6822.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199502
AB A short upstream open reading frame (uORF2) in the human cytomegalovirus (CMV) gpUL4 (gp48) transcript leader is conserved among CMV strains and inhibits translation of a downstream cistron. Remarkably, this inhibitory effect depends on the amino acid coding information of uORF2, at least in transient transfection assays in diploid human fibroblasts. Using retroviral vectors, we now report that the gp48 leader inhibits downstream translation in multiple additional cell types, even when expressed from a **stably** integrated gene, and on a transcript containing an additional kilobase of complex leader sequences. The magnitude of inhibition can be augmented approximately 3- to 10-fold by replacing the context of nucleotides flanking the wild-type initiation codon of uORF2 with an **optimal** context, suggesting that leaky scanning past the wild-type AUG codon accounts for translation of the downstream cistron. Using an in vivo mutagenesis protocol that relies on reverse transcriptase infidelity, we isolated mutants in which the inhibitory effect of the gp48 leader was inactivated as a result of alterations in the coding information of uORF2. These studies demonstrate that, independent of the cell type or expression system used, CMV gp48 uORF2 is a potent translational inhibitory element.
CT Check Tags: Animal; Human; Support, U.S. Gov't, P.H.S.
**Base Sequence**
Cells, Cultured
*Cytomegalovirus: GE, genetics
***DNA Mutational Analysis**
DNA Primers
**Genetic Vectors**
Gentamicins: PD, pharmacology
Mice
**Molecular Sequence Data**
*Retroviridae: GE, genetics
***RNA, Messenger: GE, genetics**
**RNA, Viral: GE, genetics**
Signal Transduction
**Transduction, Genetic**
***Translation, Genetic**
*Viral Envelope Proteins: GE, genetics
Viral Envelope Proteins: ME, metabolism
3T3 Cells
RN 49863-47-0 (antibiotic G 418)
CN 0 (cytomegalovirus glycoprotein 48); 0 (DNA Primers); 0 (Genetic Vectors); 0 (Gentamicins); 0 (RNA, Messenger); 0 (RNA, Viral); 0 (Viral Envelope Proteins)

L107 ANSWER 19 OF 41 MEDLINE
AN 94296662 MEDLINE
DN 94296662
TI From RNA to sequenced clones within three days: a complete protocol.
AU Simon M M; Palmetshofer A; Schwarz T
CS Ludwig Boltzmann Institute of Cellbiology and Immunobiology, University of

Munster, FRG.
SO BIOTECHNIQUES, **(1994 Apr)** 16 (4) 633-6, 638.
Journal code: AN3. ISSN: 0736-6205.
CY United States
DT Report; (TECHNICAL REPORT)
LA English
FS Priority Journals
EM 199410
AB Detection of specific mRNA transcripts by the reverse transcription/polymerase chain reaction (RT/PCR) technique has become increasingly important. The technique is fast and has a very high resolution. Cloning of these PCR fragments into vectors is sometimes necessary for identification of alternative splicing products, for bacterial expression or for generation of a DNA probe. Here we present a complete protocol for RT/PCR, cloning and sequencing of PCR, cloning and sequencing of PCR products beginning with the total RNA and ending with the DNA sequence within three days. To illustrate the procedure as an example, a fragment of the human glyceraldehyde-3-phosphate dehydrogenase mRNA was amplified from total RNA, cloned and partially sequenced. The protocol has been **optimized** for small scale to facilitate handling and to reduce costs.
CT Check Tags: Human; Support, Non-U.S. Gov't
Base Sequence
Cloning, Molecular
DNA: CH, chemistry
Escherichia coli: GE, genetics
Glyceraldehyde-3-Phosphate Dehydrogenases: GE, genetics
Molecular Sequence Data
Plasmids
*Polymerase Chain Reaction
*RNA-Directed DNA Polymerase
***RNA, Messenger: AN, analysis**
***RNA, Messenger: CH, chemistry**
***Sequence Analysis, RNA**
RN 9007-49-2 (DNA)
CN EC 1.2.1.- (Glyceraldehyde-3-Phosphate Dehydrogenases); EC 2.7.7.49 (RNA-Directed DNA Polymerase); 0 (Plasmids); 0 (RNA, Messenger)

L107 ANSWER 20 OF 41 MEDLINE
AN 94245621 MEDLINE
DN 94245621
TI Effects of transcriptional start site sequence and position on nucleotide-sensitive selection of alternative start sites at the pyrC promoter in Escherichia coli.
AU Liu J; Turnbough C L Jr
CS Department of Microbiology, University of Alabama at Birmingham 35294..
NC GM29466 (NIGMS)
SO JOURNAL OF BACTERIOLOGY, **(1994 May)** 176 (10) 2938-45.
Journal code: HH3. ISSN: 0021-9193.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199408
AB In Escherichia coli, expression of the pyrC gene is regulated primarily by a translational control mechanism based on nucleotide-sensitive selection of transcriptional start sites at the pyrC promoter. When intracellular levels of CTP are high, pyrC transcripts are initiated predominantly with CTP at a site 7 bases downstream of the Pribnow box. These transcripts form a **stable** hairpin at their 5' ends that blocks ribosome binding. When the CTP level is low and the GTP level is high, conditions found in pyrimidine-limited cells, transcripts are initiated primarily with GTP at a site 9 bases downstream of the Pribnow box. These shorter transcripts are unable to form a hairpin at their 5' ends and are readily translated. In this study, we examined the effects of nucleotide sequence and position on the selection of transcriptional start sites at the pyrC

promoter. We characterized promoter mutations that systematically alter the sequence at position 7 or 9 downstream of the Pribnow box or vary the spacing between the Pribnow box and wild-type transcriptional initiation region. The results reveal preferences for particular initiating nucleotides (ATP > or = GTP > UTP >> CTP) and for starting positions downstream of the Pribnow box (7 >> 6 and 8 > 9 > 10). The results indicate that **optimal** nucleotide-sensitive start site switching at the wild-type pyrC promoter is the result of competition between the preferred start site (position 7) that uses the poorest initiating nucleotide (CTP) and a weak start site (position 9) that uses a good initiating nucleotide (GTP).(ABSTRACT TRUNCATED AT 250 WORDS)

CT Check Tags: Comparative Study; Support, U.S. Gov't, P.H.S.
**Base Sequence**
*Dihydroorotase: GE, genetics
**DNA Mutational Analysis**
*Escherichia coli: GE, genetics
Half-Life
**Molecular Sequence Data**
Mutagenesis, Site-Directed
***Promoter Regions (Genetics): GE, genetics**
Recombinant Fusion Proteins
***RNA, Messenger: GE, genetics**
***Transcription, Genetic**
**Transformation, Genetic**

CN EC 3.5.2.3 (Dihydroorotase); 0 (Recombinant Fusion Proteins); 0 (RNA, Messenger)

GEN pyrC

L107 ANSWER 21 OF 41 MEDLINE

AN 92333663 MEDLINE

DN 92333663

TI Role of TAR RNA splicing in translational regulation of simian immunodeficiency virus from rhesus macaques.

AU Viglianti G A; Rubinstein E P; Graves K L

CS Program in Molecular Medicine, University of Massachusetts Medical Center, Worcester 01605.

SO JOURNAL OF VIROLOGY, **(1992 Aug)** 66 (8) 4824-33.
Journal code: KCV. ISSN: 0022-538X.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals; Cancer Journals

EM 199210

AB The untranslated leader sequences of rhesus macaque simian immunodeficiency virus mRNAs form a **stable** secondary structure, TAR. This structure can be modified by RNA splicing. In this study, the role of TAR splicing in virus replication was investigated. The proportion of viral RNAs containing a spliced TAR structure is high early after infection and decreases at later times. Moreover, proviruses containing mutations which prevent TAR splicing are significantly delayed in replication. These mutant viruses require approximately 20 days to achieve half-maximal virus production, in contrast to wild-type viruses, which require approximately 8 days. We attribute this delay to the inefficient translation of unspliced-TAR-containing mRNAs. The molecular basis for this translational effect was examined in in vitro assays. We found that spliced-TAR-containing mRNAs were translated up to 8.5 times more efficiently than were similar mRNAs containing an unspliced TAR leader. Furthermore, these spliced-TAR-containing mRNAs were more efficiently associated with ribosomes. We postulate that the level of TAR splicing provides a balance for the **optimal** expression of both viral proteins and genomic RNA and therefore ultimately controls the production of infectious virions.

CT Check Tags: Animal; Support, Non-U.S. Gov't
**Base Sequence**
Blotting, Western
***Gene Expression Regulation, Viral**

**Introns**
Macaca mulatta
**Molecular Sequence Data**
Nucleic Acid Conformation
Oligodeoxyribonucleotides
Plasmids
***RNA Splicing**
**RNA, Messenger: AN, analysis**
***RNA, Messenger: GE, genetics**
**RNA, Messenger: ME, metabolism**
**RNA, Viral: AN, analysis**
***RNA, Viral: GE, genetics**
**RNA, Viral: ME, metabolism**
*SIV: GE, genetics
**Transcription, Genetic**
***Translation, Genetic**
CN 0 (Oligodeoxyribonucleotides); 0 (Plasmids); 0 (RNA, Messenger); 0 (RNA, Viral)

L107 ANSWER 22 OF 41 MEDLINE
AN 92115731 MEDLINE
DN 92115731
TI An RNA pseudoknot and an **optimal** heptameric shift site are required for highly efficient ribosomal frameshifting on a retroviral messenger RNA.
AU Chamorro M; Parkin N; Varmus H E
CS Department of Microbiology and Immunology, University of California, San Francisco 94143-0502.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, **(1992 Jan 15)** 89 (2) 713-7.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199204
AB Synthesis of the pol gene products of most retroviruses requires ribosomes to shift frame once or twice in the -1 direction while translating gag-pol mRNA. The viral signals for frameshifting include a heptanucleotide sequence on which the shift occurs and higher-order RNA structure just downstream of the shift site. We have made site-directed mutations in two stems (S1 and S2) of a putative RNA pseudoknot that begins 7 nucleotides 3' of the previously identified shift site (A AAA AAC) in the gag-pro region of mouse mammary tumor virus (MMTV) RNA. The mutants confirm the predicted structure, show that loss of either S1 or S2 impairs frameshifting, and exclude alternative RNA structures as significant for frameshifting. The importance of the MMTV pseudoknot has been further demonstrated by showing that shift sites from two other retroviruses function more efficiently in the position of the MMTV site than in their native contexts. However, the MMTV pseudoknot cannot promote detectable frameshifting in the absence of a recognizable upstream shift site. In addition, the species of tRNA that reads the second codon in the shift site appears to be a critical determinant, since changing the 7th nucleotide in the MMTV gag-pro shift site from C to A, U, or G severely impairs frameshifting.
CT Check Tags: Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
**Base Sequence**
**Codon**
**DNA Mutational Analysis**
**Gene Expression Regulation**
Genes, gag
Genes, Structural, Viral
Hydrogen Bonding
*Mammary Tumor Viruses, Mouse: GE, genetics
Molecular Sequence Data
Nucleic Acid Conformation

*Ribosomes: ME, metabolism
***RNA, Messenger: GE, genetics**
**RNA, Messenger: UL, ultrastructure**
**RNA, Transfer: GE, genetics**
***RNA, Viral: GE, genetics**
**RNA, Viral: UL, ultrastructure**
*Translation, Genetic
RN 9014-25-9 (RNA, Transfer)
CN 0 (Codon); 0 (RNA, Messenger); 0 (RNA, Viral)

L107 ANSWER 23 OF 41 MEDLINE
AN 92038999 MEDLINE
DN 92038999
TI The cap and poly(A) tail function synergistically to regulate mRNA translational efficiency.
AU Gallie D R
CS Department of Biochemistry, University of California, Riverside 92521.
SO GENES AND DEVELOPMENT, **(1991 Nov)** 5 (11) 2108-16.
Journal code: FN3. ISSN: 0890-9369.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199202
AB The cap structure and the poly(A) tail are important regulatory determinants in establishing the translational efficiency of a messenger RNA. Although the mechanism by which either determinant functions remains poorly characterized, the interaction between the poly(A) tail-poly(A)-binding protein complex and events occurring at the 5' terminus during translation initiation has been an intriguing possibility. In this report, the mutual dependence of the cap and the poly(A) tail was studied. Poly(A)+ and poly(A)- luciferase (Luc) mRNAs generated in vitro containing or lacking a cap were translated in vivo in tobacco protoplasts, Chinese hamster ovary cells, and yeast following delivery by electroporation. The poly(A) tail-mediated regulation of translational efficiency was wholly dependent on the cap for function. Moreover, cap function was enhanced over an order of magnitude by the presence of a poly(A) tail. The relative differences in **stability** between the mRNAs could not account for the synergism. The synergism between the cap and poly(A) tail was not observed in yeast cells in which active translation had been disrupted. In addition, the synergism was not observed in in vitro translation lysates. These data demonstrate that the cap and the poly(A) tail are interdependent for **optimal** function in vivo and suggest that communication between the two regulatory determinants may be important in establishing efficient translation.
CT Check Tags: Animal
CHO Cells: ME, metabolism
***Gene Expression Regulation: GE, genetics**
Hamsters
Kinetics
Luciferase: GE, genetics
Plasmids: GE, genetics
*Poly A: GE, genetics
Poly A: ME, metabolism
Protoplasts: ME, metabolism
***RNA Caps: GE, genetics**
***RNA, Messenger: GE, genetics**
**RNA, Messenger: ME, metabolism**
Saccharomyces cerevisiae: ME, metabolism
Tobacco: ME, metabolism
***Translation, Genetic: GE, genetics**
RN 24937-83-5 (Poly A)
CN EC 1.13.12.- (Luciferase); 0 (Plasmids); 0 (RNA Caps); 0 (RNA, Messenger)

L107 ANSWER 24 OF 41 MEDLINE
AN 91334248 MEDLINE

DN 91334248
TI Codon usage and secondary structure of mRNA.
AU Zama M
CS Division of Biology, National Institute of Radiological Sciences, Chiba-shi, Japan..
SO NUCLEIC ACIDS SYMPOSIUM SERIES, **(1990)** (22) 93-4.
Journal code: O8N. ISSN: 0261-3166.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199111
AB The specific codon usage pattern of the repetitive unit nucleotide sequence of silk fibroin mRNA suggests that selection has operated on the codon usage to **optimize** the secondary structure characteristic of the mRNA. The correlation between the **stability** map of local secondary structure of type I collagen mRNA and the codon usage pattern and the translation rate of the collagen is also implied.
CT Check Tags: Animal
***Codon**
Evolution
Fibroin: GE, genetics
Nucleic Acid Conformation
Nucleic Acid Denaturation
**Repetitive Sequences, Nucleic Acid**
**RNA, Messenger: CH, chemistry**
***RNA, Messenger: GE, genetics**
Silkworms: GE, genetics
**Translation, Genetic**
RN 9007-76-5 (Fibroin)
CN 0 (Codon); 0 (RNA, Messenger)

L107 ANSWER 25 OF 41 MEDLINE
AN 91237810 MEDLINE
DN 91237810
TI Cowpea mosaic virus middle component RNA contains a sequence that allows internal binding of ribosomes and that requires eukaryotic initiation factor 4F for **optimal** translation.
AU Thomas A A; ter Haar E; Wellink J; Voorma H O
CS Department of Molecular Cell Biology, University of Utrecht, The Netherlands..
SO JOURNAL OF VIROLOGY, **(1991 Jun)** 65 (6) 2953-9.
Journal code: KCV. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199108
AB Cowpea mosaic virus (CPMV) middle component RNA (M-RNA) encodes two proteins of 105 and 95 kDa, of which translation starts at nucleotide (nt) 161 and nt 512, respectively. In vitro translation of both proteins directed by T7 transcripts of M-RNA was stimulated fourfold by eukaryotic initiation factor 4F (eIF-4F), the cap-binding protein complex. The ratio of the synthesis of both proteins after translation was not influenced by eIF-4F or by any known eIF. Part of the CPMV 5' sequence was cloned downstream of the 5' untranslated region of ornithine decarboxylase (ODC); the latter untranslated sequence has a highly **stable** secondary structure, preventing efficient translation of ODC. Insertion of nt 161 to 512 of CPMV M-RNA upstream of the ODC initiation codon resulted in a marked increase in ODC translation, which indicates that the CPMV sequence contains an internal ribosome-binding site. The insertion conferred stimulation by eIF-4F on ODC translation, showing that eIF-4F is able to stimulate internal initiation.
CT Check Tags: Support, Non-U.S. Gov't
**Base Sequence**
Binding Sites

*Mosaic Viruses: GE, genetics
Nucleic Acid Conformation
Ornithine Decarboxylase: GE, genetics
*Peptide Initiation Factors: GE, genetics
Plants: MI, microbiology
*Ribosomes: ME, metabolism
**RNA, Messenger: CH, chemistry**
***RNA, Messenger: ME, metabolism**
***RNA, Viral: CH, chemistry**
**Translation, Genetic**
CN EC 4.1.1.17 (Ornithine Decarboxylase); 0 (eIF-4F); 0 (Peptide Initiation Factors); 0 (RNA, Messenger); 0 (RNA, Viral)

L107 ANSWER 26 OF 41 MEDLINE
AN 91187682 MEDLINE
DN 91187682
TI The rate and specificity of a group I ribozyme are inversely affected by choice of monovalent salt.
AU Partono S; Lewin A S
CS Department of Immunology and Medical Microbiology, University of Florida College of Medicine, Gainesville 32610.
SO NUCLEIC ACIDS RESEARCH, **(1991 Feb 11)** 19 (3) 605-9.
Journal code: O8L. ISSN: 0305-1048.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199107
AB The fifth intron of the COB gene of yeast mitochondria splices autocatalytically. The rate of splicing is increased by high concentrations of monovalent salts, but the choice of both cation and anion is significant: The smaller the cation in solution, the faster the reaction (the rate in K+ greater than NH4+ greater than Na+ greater than Li+). Chloride, bromide, iodide and acetate salts enhance autocatalytic processing, but sulfate salts do not and fluoride salts are inhibitory. The choice of monovalent salt affects the KM of the intron for guanosine nucleotide, implying an alteration in the affinity of the RNA for that substrate. Under **optimal** conditions (1M KCl, 50 mM MgCl2) the catalytic efficiency of this intron exceeds that reported for the ribosomal intron from Tetrahymena, but several side reactions occur, including guanosine-addition within the downstream exon. The site of addition resembles the 5' splice junction, but selection of this site does not involve the internal guide sequence of the intron.
CT Check Tags: In Vitro
*Cations, Monovalent
*Cytochrome b: GE, genetics
**DNA Mutational Analysis**
*DNA, Mitochondrial: GE, genetics
Guanosine Triphosphate: ME, metabolism
**Introns**
Kinetics
Potassium Chloride: PD, pharmacology
***RNA Splicing**
***RNA, Catalytic: ME, metabolism**
***RNA, Fungal: ME, metabolism**
***RNA, Messenger: ME, metabolism**
*Saccharomyces cerevisiae: GE, genetics
Solvents
Substrate Specificity
RN 7447-40-7 (Potassium Chloride); 86-01-1 (Guanosine Triphosphate); 9035-37-4 (Cytochrome b)
CN 0 (Cations, Monovalent); 0 (DNA, Mitochondrial); 0 (RNA, Catalytic); 0 (RNA, Fungal); 0 (RNA, Messenger); 0 (Solvents)
GEN COB; CBP2

L107 ANSWER 27 OF 41 MEDLINE

AN 91159622 MEDLINE
DN 91159622
TI Human interleukin-3 mRNA accumulation is controlled at both the transcriptional and posttranscriptional level.
AU Ryan G R; Milton S E; Lopez A F; Bardy P G; Vadas M A; Shannon M F
CS Institute of Medical and Veterinary Science, Adelaide, South Australia..
NC CA45822 (NCI)
SO BLOOD, **(1991 Mar 15)** 77 (6) 1195-202.
Journal code: A8G. ISSN: 0006-4971.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199106
AB Interleukin-3 (IL-3) is a hematopoietic growth factor that regulates the differentiation of multilineage and committed progenitor cells and the functions of some mature blood cells. The expression of human IL-3 appears to be restricted to stimulated T lymphocytes. We have investigated the kinetics and mechanisms involved in the induction of IL-3 expression in the human T lymphocytic tumor cell line Jurkat. We show that accumulation of IL-3 mRNA is controlled at both the transcriptional and posttranscriptional level. Transcription of the IL-3 gene in these cells appears to be constitutive but no IL-3 mRNA was detected in unstimulated cells, indicating that in resting cells IL-3 mRNA is highly unstable. Treatment with phytohemagglutinin (PHA) induced a small and transient increase in the IL-3 gene transcription rate and led to the production of detectable levels of IL-3 mRNA and protein. **Optimal** induction of IL-3 expression required a second stimulus. Costimulation of Jurkat cells with both phorbol myristate acetate and PHA caused both a transient increase in IL-3 gene transcription, which is dependent on new protein synthesis, and also a transient increase in mRNA **stability.**
CT Check Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Cell Line
**Gene Expression Regulation, Neoplastic: DE, drug effects**
**Gene Expression Regulation, Neoplastic: PH, physiology**
*Interleukin-3: GE, genetics
Interleukin-3: ME, metabolism
Lymphoma, T-Cell: ME, metabolism
Lymphoma, T-Cell: PA, pathology
Phytohemagglutinins: PD, pharmacology
***RNA, Messenger: GE, genetics**
**RNA, Messenger: ME, metabolism**
T-Lymphocytes: ME, metabolism
T-Lymphocytes: PA, pathology
Tetradecanoylphorbol Acetate: PD, pharmacology
Time Factors
**Transcription, Genetic: DE, drug effects**
***Transcription, Genetic: GE, genetics**
RN 16561-29-8 (Tetradecanoylphorbol Acetate)
CN 0 (Interleukin-3); 0 (RNA, Messenger)

L107 ANSWER 28 OF 41 MEDLINE
AN 91141512 MEDLINE
DN 91141512
TI Involvement of long terminal repeat U3 sequences overlapping the transcription control region in human immunodeficiency virus type 1 mRNA 3' end formation.
AU DeZazzo J D; Kilpatrick J E; Imperiale M J
CS Department of Microbiology and Immunology, University of Michigan Medical School, Ann Arbor 48109-0620.
NC GM34902 (NIGMS)
SO MOLECULAR AND CELLULAR BIOLOGY, **(1991 Mar)** 11 (3) 1624-30.
Journal code: NGY. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English

FS Priority Journals
EM 199105
AB In retroviral proviruses, the poly(A) site is present in both long terminal repeats (LTRs) but used only in the 3' position. One mechanism to account for this selective poly(A) site usage is that LTR U3 sequences, transcribed only from the 3' poly(A) site, are required in the RNA for efficient processing. To test this possibility, mutations were made in the human immunodeficiency virus type 1 (HIV-1) U3 region and the mutated LTRs were inserted into simple and complex transcription units. HIV-1 poly(A) site usage was then quantitated by S1 nuclease analysis following transfection of each construct into human 293 cells. The results showed that U3 sequences confined to the transcription control region were required for efficient usage of the HIV-1 poly(A) site, even when it was placed 1.5 kb from the promoter. Although the roles of U3 in processing and transcription activation were separable, **optimal** 3' end formation was partly dependent on HIV-1 enhancer and SP1 binding site sequences.
CT Check Tags: Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Cloning, Molecular
**DNA Mutational Analysis**
***HIV Long Terminal Repeat: GE, genetics**
*HIV-1: GE, genetics
Poly A: GE, genetics
***Regulatory Sequences, Nucleic Acid**
**RNA Processing, Post-Transcriptional**
***RNA, Messenger: GE, genetics**
***RNA, Viral: GE, genetics**
RN 24937-83-5 (Poly A)
CN 0 (RNA, Messenger); 0 (RNA, Viral)

L107 ANSWER 29 OF 41 MEDLINE
AN 91116825 MEDLINE
DN 91116825
TI Combined use of in situ hybridization and unlabeled antibody peroxidase anti-peroxidase methods: simultaneous detection of type I procollagen mRNAs and factor VIII-related antigen epitopes in keloid tissue.
AU Sollberg S; Peltonen J; Uitto J
CS Department of Dermatology, Jefferson Medical College, Thomas Jefferson University, Philadelphia, Pennsylvania..
NC AR-28450 (NIAMS)
GM-28833 (NIGMS)
T32 AR-7561 (NIAMS)
SO LABORATORY INVESTIGATION, **(1991 Jan)** 64 (1) 125-9.
Journal code: KZ4. ISSN: 0023-6837.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199105
AB In this study, we developed methodology that allows the combined use of in situ hybridization and peroxidase anti-peroxidase techniques on the same tissue section. A human pro alpha 1(I) collagen cDNA and antibodies to factor VIII-related antigen were used on keloid tissue sections as a model for a fibrotic reaction. The basic protocols of the techniques were modified to obtain **optimal** results. The feasibility of this new method was demonstrated by elucidation of type I procollagen gene expression in the cells of blood vessel wall and the adjacent fibroblasts. In the case of capillaries, pro alpha 1(I) collagen mRNAs were detected within endothelial cells identified by the presence of factor VIII-related antigen. Pro alpha 1(I) collagen mRNAs were also found in close proximity of medium-size blood vessels, but in this context clearly outside the vessel wall. These results may contribute to the understanding of pathogenetic aspects of keloids and other fibrotic conditions. Thus, the combination of in situ hybridization and peroxidase anti-peroxidase techniques provides a useful tool to examine gene expression simultaneously both at mRNA and protein levels in fibrotic tissues. This

methodology is also applicable to a variety of other biologic and pathologic situations.
CT Check Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
DNA: GE, genetics
Epitopes
***Factor VIII: IM, immunology**
Fibrosis
**Gene Expression**
Immunoenzyme Techniques
Keloid: IM, immunology
*Keloid: ME, metabolism
Keloid: PA, pathology
Nucleic Acid Hybridization
Procollagen: GE, genetics
*Procollagen: ME, metabolism
***RNA, Messenger: GE, genetics**
RN **9001-27-8 (Factor VIII)**; 9007-49-2 (DNA)
CN 0 (Epitopes); 0 (Procollagen); 0 (RNA, Messenger)

L107 ANSWER 30 OF 41 MEDLINE
AN 91036044 MEDLINE
DN 91036044
TI Induction and regulation of class II major histocompatibility complex mRNA expression in astrocytes by interferon-gamma and tumor necrosis factor-alpha.
AU Vidovic M; Sparacio S M; Elovitz M; Benveniste E N
CS Department of Neurology, University of Alabama, Birmingham 35294..
NC AM 20614 (NIADDK)
SO JOURNAL OF NEUROIMMUNOLOGY, **(1990 Dec)** 30 (2-3) 189-200.
Journal code: HSO. ISSN: 0165-5728.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199102
AB Astrocytes can function as antigen-presenting cells (APC) upon expression of class II major histocompatibility complex (MHC) antigens, which are induced by interferon-gamma (IFN-gamma). Previous data from this laboratory had shown that the cytokine tumor necrosis factor-alpha (TNF-alpha) enhances IFN-gamma-mediated class II antigen expression on astrocytes. We have now investigated the effect of IFN-gamma and TNF-alpha on class II MHC mRNA expression in astrocytes using Northern blot analysis. Astrocytes do not constitutively express mRNA for class II MHC. Kinetic analysis of class II MHC mRNA expression in IFN-gamma-treated cells demonstrated an 8 h time lag, which was followed by an increase over the next 16 h. **Optimal** expression of class II mRNA was detected after a 24 h incubation with IFN-gamma. This level of expression was further enhanced by the simultaneous addition of IFN-gamma and TNF-alpha to the astrocytes, while TNF-alpha alone had no effect on class II mRNA expression. TNF-alpha does not act by increasing the **stability** of IFN-gamma-induced class II mRNA, indicating its action is not at that specific level of post-transcriptional control. Furthermore, astrocyte class II mRNA expression was inhibited when cycloheximide (CHX) was added together with IFN-gamma or IFN-gamma/TNF-alpha, and when CHX was added up to 4 h after treatment with IFN-gamma or IFN-gamma/TNF-alpha. These results indicate that astrocyte class II mRNA expression is mediated by newly synthesized proteins induced by IFN-gamma and/or IFN-gamma/TNF-alpha. The expression of class II antigens on astrocytes, and cytokine modulation of their expression, may be important in the initiation and perpetuation of intracerebral immune responses.
CT Check Tags: Animal; Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.
Astrocytes: DE, drug effects
*Astrocytes: IM, immunology
***Gene Expression Regulation: DE, drug effects**
*Histocompatibility Antigens Class II: GE, genetics

Histocompatibility Antigens Class II: IM, immunology
*Interferon Type II: PD, pharmacology
Rats
Recombinant Proteins: PD, pharmacology
***RNA, Messenger: IM, immunology**
*Tumor Necrosis Factor: PD, pharmacology
RN 82115-62-6 (Interferon Type II)
CN 0 (Histocompatibility Antigens Class II); 0 (Recombinant Proteins); 0 (RNA, Messenger); 0 (Tumor Necrosis Factor)

L107 ANSWER 31 OF 41 MEDLINE
AN 91007260 MEDLINE
DN 91007260
TI Purification and characterization of pre-mRNA splicing factor SF2 from HeLa cells.
AU Krainer A R; Conway G C; Kozak D
CS Cold Spring Harbor Laboratory, New York 11724.
NC GM-42699 (NIGMS)
CA-13106 (NCI)
SO GENES AND DEVELOPMENT, **(1990 Jul)** 4 (7) 1158-71.
Journal code: FN3. ISSN: 0890-9369.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199101
AB SF2, an activity necessary for 5' splice site cleavage and lariat formation during pre-mRNA splicing in vitro, has been purified to near homogeneity from HeLa cells. The purest fraction contains only two related polypeptides of 33 kD. This fraction is sufficient to complement an S100 fraction, which contains the remaining splicing factors, to splice several pre-mRNAs. The **optimal** amount of SF2 required for efficient splicing depends on the pre-mRNA substrate. SF2 is distinct from the hnRNP A1 and U1 snRNP a polypeptides, which are similar in size. Endogenous hnRNA copurifies with SF2, but this activity does not appear to have an essential RNA component. SF2 appear to be necessary for the assembly or **stabilization** of the earliest specific prespliceosome complex, although in the absence of other components, it can bind RNA in a nonspecific manner. SF2 copurifies with an activity that promotes the annealing of complementary RNAs. Thus, SF2 may promote specific RNA-RNA interactions between snRNAs and pre-mRNA, between complementary snRNA regions, and/or involving intramolecular pre-mRNA helices. Other purified proteins with RNA annealing activity cannot substitute for SF2 in the splicing reaction.
CT Check Tags: Comparative Study; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
*Hela Cells: CH, chemistry
**Introns**
*Nuclear Proteins: IP, isolation & purification
Nuclear Proteins: PH, physiology
Nucleic Acid Conformation
Ribonucleoproteins: ME, metabolism
***RNA Precursors: ME, metabolism**
***RNA Splicing**
***RNA, Messenger: BI, biosynthesis**
CN 0 (heterogeneous-nuclear ribonucleoproteins); 0 (splicing factor 2); 0 (Nuclear Proteins); 0 (Ribonucleoproteins); 0 (Ribonucleoproteins, Small Nuclear); 0 (RNA Precursors); 0 (RNA, Messenger)

L107 ANSWER 32 OF 41 MEDLINE
AN 91006076 MEDLINE
DN 91006076
TI Translational control by cytoplasmic polyadenylation during Xenopus oocyte maturation: characterization of cis and trans elements and regulation by cyclin/MPF.
AU McGrew L L; Richter J D

CS Worcester Foundation for Experimental Biology, Shrewsbury, MA 01545..
SO EMBO JOURNAL, **(1990 Nov)** 9 (11) 3743-51.
Journal code: EMB. ISSN: 0261-4189.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199101
AB The expression of certain maternal mRNAs during oocyte maturation is regulated by cytoplasmic polyadenylation. To understand this process, we have focused on a maternal mRNA from Xenopus termed G10. This mRNA is stored in the cytoplasm of stage 6 oocytes until maturation when the process of poly(A) elongation stimulates its translation. Deletion analysis of the 3' untranslated region of G10 RNA has revealed that two sequence elements, UUUUUUAU and AAUAAA were both necessary and sufficient for polyadenylation and polysomal recruitment. In this communication, we have defined the U-rich region that is **optimal** for polyadenylation as UUUUUUAUAAAG, henceforth referred to as the cytoplasmic polyadenylation element (CPE). We have also identified unique sequence requirements in the 3' terminus of the RNA that can modulate polyadenylation even in the presence of wild-type cis elements. A time course of cytoplasmic polyadenylation in vivo shows that it is an early event of maturation and that it requires protein synthesis within the first 15 min of exposure to progesterone. MPF and cyclin can both induce polyadenylation but, at least with respect to MPF, cannot obviate the requirement for protein synthesis. To identify factors that may be responsible for maturation-specific polyadenylation, we employed extracts from oocytes and unfertilized eggs, the latter of which correctly polyadenylates exogenously added RNA. UV crosslinking demonstrated that an 82 kd protein binds to the U-rich CPE in egg, but not oocyte, extracts. The data suggest that progesterone, either in addition to or through MPF/cyclin, induces the synthesis of a factor during very early maturation that stimulates polyadenylation.(ABSTRACT TRUNCATED AT 250 WORDS)
CT Check Tags: Animal; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.
**Base Sequence**
Carrier Proteins: PH, physiology
Cyclins: PH, physiology
Cycloheximide: PD, pharmacology
Cytoplasm: ME, metabolism
**DNA Mutational Analysis**
***Gene Expression Regulation**
Maturation-Promoting Factor: ME, metabolism
Molecular Sequence Data
*Oocytes: PH, physiology
*Poly A: ME, metabolism
Polyribosomes: ME, metabolism
Progesterone: PD, pharmacology
**Regulatory Sequences, Nucleic Acid**
**RNA Processing, Post-Transcriptional**
**RNA, Messenger: GE, genetics**
***RNA, Messenger: ME, metabolism**
*Translation, Genetic
*Xenopus laevis: PH, physiology
RN 24937-83-5 (Poly A); 57-83-0 (Progesterone); 66-81-9 (Cycloheximide)
CN 0 (Carrier Proteins); 0 (Cyclins); 0 (Maturation-Promoting Factor); 0 (RNA-Binding Proteins); 0 (RNA, Messenger)

L107 ANSWER 33 OF 41 MEDLINE
AN 90356586 MEDLINE
DN 90356586
TI Amplification of mRNA of the hprt gene from lysates of mutant human cells and direct DNA sequencing to determine the spectrum of mutations induced by (+/-)-7 beta,8 alpha-dihydroxy-9 alpha,10 alpha, epoxy-7,8,9,10-tetrahydrobenzo[a]pyrene.
AU Maher V M; Yang J L; McCormick J J

CS Department of Microbiology, Michigan State University, East Lansing 48824..
NC CA21253 (NCI)
ER60524
SO PROGRESS IN CLINICAL AND BIOLOGICAL RESEARCH, **(1990)** 340A 379-88.
Journal code: PZ5. ISSN: 0361-7742.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199011
AB Strong evidence points to mutation induction as one mechanism by which changes are introduced into normal cells to convert them into cancer cells. To understand the mechanisms by which mutations are induced in human cells by carcinogens, we are determining the kinds and spectra of mutations induced in the coding region of the hypoxanthine(guanine)phosphoribosyltransferase (hprt) gene. This region, composed of 654 bp, represents nine exons from a 44 kbp gene. To be able to analyze a large number of independent mutants rapidly and economically, we have **optimized** the conditions for copying mRNA directly from lysates of a small number of cells (e.g., 100) from a 6-thioguanine-resistant clone using reverse transcriptase and oligo(dT)12-18 primers. Then two 20-mer primers, specific for the cDNA of the hprt gene, are used to amplify the first and second strand cDNA 5 x 10(7)-fold during 30 cycles of polymerase chain reaction (PCR). The product (2 to 10 ng) is then purified by ultrafiltration, diluted 1:10, and subjected to an additional 30 cycles of PCR, using two 20-mer primers located just interior to the first set. The amplification product, 5 to 10 ug, is sequenced directly using three other end-labeled primers and Sequenase. To date, we have analyzed 26 mutants induced by (+-)-7 beta,8 alpha-dihydroxy-9 alpha,10 alpha,epoxy-7,8,9,10-tetrahydrobenzo [a]pyrene and found that 24/26 involved base substitutions. 97% of these involved G.C, predominantly G.C----T.A, distributed over seven exons, with many of the substitutions located in exon 3.
CT Check Tags: Comparative Study; Human; Support, U.S. Gov't, P.H.S.
***Base Sequence**
Clone Cells: AN, analysis
*Dihydroxydihydrobenzopyrenes: PD, pharmacology
DNA: GE, genetics
***DNA Mutational Analysis**
DNA, Recombinant: AN, analysis
Fibroblasts: AN, analysis
Fibroblasts: DE, drug effects
*Hypoxanthine Phosphoribosyltransferase: GE, genetics
Polymerase Chain Reaction
***RNA, Messenger: GE, genetics**
*7,8-Dihydro-7,8-dihydroxybenzo(a)pyrene 9,10-oxide: PD, pharmacology
RN 55097-80-8 (7,8-Dihydro-7,8-dihydroxybenzo(a)pyrene 9,10-oxide); 9007-49-2 (DNA)
CN EC 2.4.2.8 (Hypoxanthine Phosphoribosyltransferase); 0 (Dihydroxydihydrobenzopyrenes); 0 (DNA, Recombinant); 0 (RNA, Messenger)

L107 ANSWER 34 OF 41 MEDLINE
AN 90211260 MEDLINE
DN 90211260
TI Codon usage pattern in alpha 2(I) chain domain of chicken type I collagen and its implications for the secondary structure of the mRNA and the synthesis pauses of the collagen.
AU Zama M
CS Biology Division, National Institute of Radiological Sciences, Chiba-shi, Japan..
SO BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, **(1990 Mar 16)** 167 (2) 772-6.
Journal code: 9Y8. ISSN: 0006-291X.
CY United States

DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199007
AB A **stability** map of local secondary structure of the mRNA of the triple-helical alpha 2(I) chain domain of chicken type I collagen was obtained by plotting the free energy of the **optimal** secondary structure of a local segment in mRNA against the segment position along a base sequence of the mRNA. It was found that the positions of the minima of free energy in the plot coincide with the positions where synthesis pauses of the alpha-chain polypeptides of the corresponding sizes translated from the mRNA have been reported to occur (1). The codon usage pattern of each of the three major amino acids of the alpha-chain domain of the collagen, Gly, Pro and Ala, fluctuates considerably along the base sequence segments of the mRNA and a deviation of the pattern from that of the average of the whole alpha 2(I) chain domain mRNA, particularly for Gly codons, leads to a loss of the **stability** of the local secondary structure of the mRNA. The results suggest that selection has operated on the codon usage to **optimize** the secondary structure characteristic of the mRNA of the chicken collagen alpha 2(I) chain domain which leads to a nonuniform polypeptide elongation pattern.
CT Check Tags: Animal
Chickens
***Codon: GE, genetics**
Collagen: BI, biosynthesis
*Collagen: GE, genetics
***Genes, Structural**
Macromolecular Systems
*Nucleic Acid Conformation
*Procollagen: GE, genetics
***RNA, Messenger: GE, genetics**
RN 9007-34-5 (Collagen)
CN 0 (Codon); 0 (Macromolecular Systems); 0 (Procollagen); 0 (RNA, Messenger)

L107 ANSWER 35 OF 41 MEDLINE
AN 90101372 MEDLINE
DN 90101372
TI Changing the start codon context of the 30K gene of tobacco mosaic virus from "weak" to "strong" does not increase expression.
AU Lehto K; Dawson W O
CS Department of Plant Pathology, University of California, Riverside 92521..
SO VIROLOGY, **(1990 Jan)** 174 (1) 169-76.
Journal code: XEA. ISSN: 0042-6822.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199004
AB The translation initiation region of the 30K gene of tobacco mosaic virus (TMV) was modified by in vitro mutagenesis to create more **optimal** start codon contexts. A complicating factor was that modifications in this region also altered the 3' terminus of the 183K ORF that overlaps the 30K ORF. An insertion of GACUCGA between nucleotides 4901 and 4902 resulted in a purine (G) in position -3 relative to the AUG creating a "stronger" start codon context, but this also changed the last four amino acids of the 183K protein. This mutant was infectious, replicated efficiently, but produced reduced amounts of 30K protein. Despite the reduced amount of movement protein, this mutant spread effectively from cell to cell and had a phenotype indistinguishable from that of wild-type virus. A more conservative mutation inserted GAC between TMV nucleotides 4901 and 4902 resulting in a "strong" start codon context (ACGAUGG) and modification of the 183K protein only by insertion of an aspartic acid adjacent to a native aspartic acid. This modification did not enhance the production of 30K protein. These data demonstrate consensus sequences that are **optimal** for other eukaryotic systems did not cause increased expression of the 30K gene in vivo. The modified sequences of both mutants

were **stably** maintained during relatively long periods of replication. Even though each mutant replicated efficiently, when mixed with wild-type TMV, neither mutant effectively competed with the wild-type virus. Another mutant which removed the native 30K AUG to determine whether subsequent internal start codons with "stronger" contexts would function in its absence was constructed. However, this mutant and a mutant that fused the 183K reading frame to the 30K reading frame did not replicate and move in intact plants.

CT Check Tags: Support, U.S. Gov't, Non-P.H.S.
**Base Sequence**
Blotting, Western
***Codon: GE, genetics**
***Gene Expression Regulation, Viral**
**Molecular Sequence Data**
**Mutation**
***RNA, Messenger: GE, genetics**
***RNA, Viral: GE, genetics**
*Tobacco Mosaic Virus: GE, genetics
Tobacco Mosaic Virus: PH, physiology
**Transcription, Genetic**
**Translation, Genetic**
Virus Replication

CN 0 (Codon); 0 (RNA, Messenger); 0 (RNA, Viral)

L107 ANSWER 36 OF 41 MEDLINE
AN 90034173 MEDLINE
DN 90034173
TI Mature apolipoprotein AI and its precursor proApoAI: influence of the sequence at the 5' end of the gene on the efficiency of expression in Escherichia coli.
AU Isacchi A; Sarmientos P; Lorenzetti R; Soria M
CS Department of Biotechnology, Farmitalia Carlo Erba, Milano, Italy..
SO GENE, **(1989 Sep 1)** 81 (1) 129-37.
Journal code: FOP. ISSN: 0378-1119.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199002
AB Apolipoprotein AI (ApoAI) plays a central role in the regulation of lipid metabolism. Initial attempts to express human apoAI cDNA in Escherichia coli did not yield detectable levels of the mature protein. By analyzing the efficiency of expression of apoAI-lacZ gene fusions, we have been able to show that the sequence at the 5' end of the ApoAI-coding region is a critical parameter. Indeed, silent changes in the codons for the first 8 residues of ApoAI, which did not alter the amino acid sequence, affected expression dramatically. Analysis of the corresponding mRNA steady-state levels suggested a role for differential mRNA **stability** in the control of apoAI expression in this system. Among all the possible alternative sequences, we have identified an **optimal** sequence which, when reinserted in the original expression plasmid, yields high level production of mature ApoAI. This procedure has been extended to the production of the natural variant ApoAI-Milano and the precursor proApoAI. Availability of these recombinant molecules would allow the investigation of their structural and biological features. In addition, the methodology used to **optimize** ApoAI expression is of general interest in assuring high expression of heterologous proteins in E. coli.

CT **Amino Acid Sequence**
Apolipoproteins A: BI, biosynthesis
*Apolipoproteins A: GE, genetics
**Base Sequence**
Blotting, Western
Cloning, Molecular
*Escherichia coli: GE, genetics
**Genes, Bacterial**
**Mutation**

Oligodeoxyribonucleotides
Plasmids
*Protein Precursors: GE, genetics
Recombinant Proteins: BI, biosynthesis
Recombinant Proteins: GE, genetics
Restriction Mapping
***RNA, Messenger: ME, metabolism**
CN 0 (pro-apolipoprotein A-I); 0 (Apolipoprotein A-I); 0 (Apolipoproteins A); 0 (Oligodeoxyribonucleotides); 0 (Plasmids); 0 (Protein Precursors); 0 (Recombinant Proteins); 0 (RNA, Messenger)

L107 ANSWER 37 OF 41 MEDLINE
AN 89289712 MEDLINE
DN 89289712
TI Effect of spermine on the efficiency and fidelity of the codon-specific binding of tRNA to the ribosomes.
AU Naranda T; Kucan Z
CS Department of Chemistry, Faculty of Science, University of Zagreb, Jugoslavija..
SO EUROPEAN JOURNAL OF BIOCHEMISTRY, **(1989 Jun 15)** 182 (2) 291-7.
Journal code: EMZ. ISSN: 0014-2956.
CY GERMANY, WEST: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198910
AB Binding of the yeast Tyr-tRNA and Phe-tRNA to the A site, and the binding of their acetyl derivatives to the P site of poly(U11,A)-programmed Escherichia coli ribosomes was studied. Spermine stimulated the rate of binding of both tRNAs at least threefold, enabling more than 90% final saturation of both ribosomal binding sites. The effect is observed when the tRNAs, but not ribosomes or poly(U11,A), are preincubated with polyamine. Regardless of the binding site, **optimal** saturation was reached at spermine/tRNA molar ratios of 3 for tRNA(Phe) and 5 for tRNA(Tyr). The same low spermine/tRNA ratios were previously reported to **stabilize** the conformation of these tRNAs in solution. On the other hand, the messenger-free, EF-Tu- and EF-G-dependent polymerization of lysine from E. coli Lys-tRNA is drastically reduced, while the poly(A)-directed polymerization is stimulated by spermine through a wide range of Mg2+ concentrations. Misreading of UUU codons as isoleucine, assayed by the A-site binding of E. coli Ile-tRNA, is also inhibited by spermine. All these results demonstrate that spermine increases the efficiency and accuracy of a series of macromolecular interactions leading to the correct incorporation of an amino acid into protein, at the same time preventing some unspecific or erroneous interactions. From the analogy with its known structural effects, it can be inferred that spermine does so by conferring on the tRNA a specific biologically functional conformation.
CT Binding Sites
***Codon: ME, metabolism**
Escherichia coli: ME, metabolism
Poly U: ME, metabolism
***RNA, Messenger: ME, metabolism**
***RNA, Ribosomal: ME, metabolism**
***RNA, Transfer: ME, metabolism**
**RNA, Transfer, Phe: ME, metabolism**
**RNA, Transfer, Tyr: ME, metabolism**
*Spermine: PD, pharmacology
Time Factors
Yeasts: ME, metabolism
RN 27416-86-0 (Poly U); 71-44-3 (Spermine); 9014-25-9 (RNA, Transfer)
CN 0 (Codon); 0 (RNA, Messenger); 0 (RNA, Ribosomal); 0 (RNA, Transfer, Phe); 0 (RNA, Transfer, Tyr)

L107 ANSWER 38 OF 41 MEDLINE
AN 89130941 MEDLINE

DN 89130941
TI Control of reovirus messenger RNA translation efficiency by the regions upstream of initiation codons.
AU Roner M R; Gaillard R K Jr; Joklik W K
CS Department of Microbiology and Immunology, Duke University Medical Center, Durham, North Carolina 27710.
NC RO1 AI 08909 (NIAID)
1PO1 CA 30246 (NCI)
5T 32 AI 07148 (NIAID)
SO VIROLOGY, **(1989 Feb)** 168 (2) 292-301.
Journal code: XEA. ISSN: 0042-6822.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198905
AB The 10 species of reovirus messenger RNA are translated in vivo with efficiencies/frequencies that differ by as much as 100-fold. The s1 mRNA, which is translated 10 times less efficiently than the s4 mRNA but 10 times more efficiently than the/1 and m1 mRNAs, has a unique BamH1 cleavage site located immediately downstream of its initiation codon. Because the reovirus mRNAs have been cloned, this provides the opportunity for placing modified and altered sequences upstream of its coding sequence. The translation efficiencies of the variant mRNAs, transcribed via the SP6 in vitro transcription system, can then be measured in the rabbit reticulocyte lysate in vitro translation system. Using this system it was found that replacing the 5'-upstream sequence of the s1 mRNA with that of the s4 mRNA increases its in vitro translation efficiency by 4-fold; that the trinucleotide immediately upstream of the s1 initiation codon renders it very weak, and that it is only slightly superior to the weakest Kozak consensus sequence; that the nature of the nucleotides further upstream than position -3 can profoundly affect translation efficiency; that the nature of this effect is in turn markedly modified by the nature of nucleotides in positions -1 to -3; and that there is a minimum **optimal** 5'-upstream sequence length of about 14 nucleotides. We also investigated the effect of secondary structure involvement on the ability of 5'-upstream sequences to promote translation. Two effects were noted. First, being part of moderately **stable** stem loops (delta G, -18 kcal/mol) decreased translation efficiency about 3-fold; second, mRNA in which only three 5'-terminal nucleotides were unpaired were translated five times less efficiently than mRNA in which six nucleotides were unpaired. Accessibility of the 5'-cap as well as secondary structure of the 5'-upstream sequences are therefore factors that affect translation efficiency. Finally, we showed that the m1 mRNA, which is transcribed very poorly in vivo, is translated very efficiently in vitro; and that its 5'-upstream sequence is as effective in increasing protein sigma 1 formation as that of s4 mRNA. Since both m1 mRNA and protein mu 2 are **stable** in infected cells, the reason why m1 mRNA is translated so inefficiently in vivo therefore remains unexplained.
CT Check Tags: Support, U.S. Gov't, P.H.S.
**Codon**
**Genes, Viral**
Nucleic Acid Conformation
*Reoviridae: GE, genetics
*Reovirus 3: GE, genetics
***RNA, Messenger: GE, genetics**
**RNA, Viral: GE, genetics**
***Translation, Genetic**
CN 0 (Codon); 0 (RNA, Messenger); 0 (RNA, Viral)

L107 ANSWER 39 OF 41 MEDLINE
AN 89098942 MEDLINE
DN 89098942
TI Presence of the hypermodified nucleotide N6-(delta 2-isopentenyl)-2-methylthioadenosine prevents codon misreading by Escherichia coli

phenylalanyl-transfer RNA.
AU Wilson R K; Roe B A
CS Department of Chemistry and Biochemistry, University of Oklahoma, Norman 73019.
NC GM30400 (NIGMS)
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, **(1989 Jan)** 86 (2) 409-13.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198904
AB The overall structure of transfer RNA is **optimized** for its various functions by a series of unique post-transcriptional nucleotide modifications. Since many of these modifications are conserved from prokaryotes through higher eukaryotes, it has been proposed that most modified nucleotides serve to **optimize** the ability of the tRNA to accurately interact with other components of the protein synthesizing machinery. When a cloned synthetic Escherichia coli tRNAPhe gene was transfected into a bacterial host that carried a defective phenylalanine tRNA-synthetase gene, tRNAPhe was overexpressed by 11-fold. As a result of this overexpression, an undermodified tRNAPhe species was produced that lacked only N6-(delta 2-isopentenyl)-2-methylthioadenosine (ms2i6A), a hypermodified nucleotide found immediately 3' to the anticodon of all major E. coli tRNAs that read UNN codons. To investigate the role of ms2i6A in E. coli tRNA, we compared the aminoacylation kinetics and in vitro codon-reading properties of the ms2i6A-lacking and normal fully modified tRNAPhe species. The results of these experiments indicate that while ms2i6A is not required for normal aminoacylation of tRNAPhe, its presence **stabilizes** codon-anticodon interaction and thereby prevents misreading of the genetic code.
CT Check Tags: Support, U.S. Gov't, P.H.S.
*Adenosine: AA, analogs & derivatives
**Amino Acid Sequence**
**Base Sequence**
Chromatography, Thin Layer
Cloning, Molecular
***Codon: GE, genetics**
*Escherichia coli: GE, genetics
Fractionation
**Gene Expression Regulation**
*Isopentenyladenosine: AA, analogs & derivatives
Isopentenyladenosine: GE, genetics
Isopentenyladenosine: ME, metabolism
Kinetics
**Molecular Sequence Data**
Phenylalanine-tRNA Ligase: GE, genetics
***RNA Processing, Post-Transcriptional**
***RNA, Messenger: GE, genetics**
***RNA, Transfer, Amino Acid-Specific: ME, metabolism**
**RNA, Transfer, Phe: BI, biosynthesis**
**RNA, Transfer, Phe: GE, genetics**
**RNA, Transfer, Phe: IP, isolation & purification**
***RNA, Transfer, Phe: ME, metabolism**
**Transcription, Genetic**
**Translation, Genetic**
RN 20859-00-1 (2-methylthio-N-6-isopentenyladenosine); 58-61-7 (Adenosine); 7724-76-7 (Isopentenyladenosine)
CN EC 6.1.1.20 (Phenylalanine-tRNA Ligase); 0 (Codon); 0 (RNA, Messenger); 0 (RNA, Transfer, Amino Acid-Specific); 0 (RNA, Transfer, Phe)

L107 ANSWER 40 OF 41 MEDLINE
AN 85037936 MEDLINE
DN 85037936
TI The influence of mRNA primary and secondary structure on human IFN-gamma

gene expression in E. coli.
AU Tessier L H; Sondermeyer P; Faure T; Dreyer D; Benavente A; Villeval D; Courtney M; Lecocq J P
SO NUCLEIC ACIDS RESEARCH, **(1984 Oct 25)** 12 (20) 7663-75.
Journal code: O8L. ISSN: 0305-1048.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198502
AB Parameters influencing the efficiency of expression of the human immune interferon (IFN-gamma) gene in E. coli were studied by comparing a series of eight in vitro-derived gene variants. These contained all possible combinations of silent mutations in the first three codons of the mature IFN-gamma polypeptide coding sequence. Expression levels varied up to 50-fold among the different constructions. Comparison of messenger RNA secondary structure models for each variant suggested that the presence of stem-loop structures blocking the translation initiation signals could drastically decrease the efficiency of IFN-gamma synthesis. With variants displaying no **stable** mRNA secondary structure in the region, a C----U transition at position +11 after the AUG resulted in a 5-fold increase in expression indicating that RNA primary structure also plays an important role in expression. In addition we demonstrate that, in this system, a spacing of 8 nucleotides between the Shine-Dalgarno region and AUG was **optimal** for gene expression and that the steady-state production level of IFN-gamma rose exponentially with increasing rate of synthesis.
CT Check Tags: Human; Support, Non-U.S. Gov't
**Base Sequence**
*Cloning, Molecular
DNA: IP, isolation & purification
DNA Restriction Enzymes
*Escherichia coli: GE, genetics
***Genes, Structural**
*Interferon Type II: GE, genetics
Nucleic Acid Conformation
***RNA, Messenger: GE, genetics**
Software
RN 82115-62-6 (Interferon Type II); 9007-49-2 (DNA)
CN EC 3.1.21 (DNA Restriction Enzymes); 0 (RNA, Messenger)

L107 ANSWER 41 OF 41 MEDLINE
AN 84170253 MEDLINE
DN 84170253
TI Identification of cDNA clones encoding secretory isoenzyme forms: sequence determination of canine pancreatic prechymotrypsinogen 2 mRNA.
AU Pinsky S D; LaForge K S; Luc V; Scheele G
NC AMDD 18532
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, **(1983 Dec)** 80 (24) 7486-90.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-K01173
EM 198407
AB A cDNA library has been constructed from canine poly(A)+ mRNA. Clones containing cDNA inserts coding for prechymotrypsinogen 2 (isoelectric point = 7.1; Mr = 27,500), one of three canine pancreatic isoenzyme forms, were selected by colony hybridization using a cDNA probe synthesized from immunoselected prechymotrypsinogen 2 mRNA. To verify that cDNA clones code for prechymotrypsinogen 2 forms that translocate across rough endoplasmic reticulum membranes and fold into **stable** and identifiable secretory proteins, we conducted in vitro translation of hybrid-selected mRNA in the presence of microsomal membranes and **optimal**

concentrations of glutathione and analyzed nascent translation products in their nonreduced state by two-dimensional isoelectric focusing/NaDodSO4 gel electrophoresis and fluorography. A near full-length chymotrypsinogen 2 cDNA and its primed extension were used to determine the nucleotide sequence for the entire coding region of prechymotrypsinogen 2 mRNA and 87 residues, including a poly(A) addition signal, in the 3' nontranslated region. The deduced amino acid sequence shows a 263-residue presecretory protein containing an 18-residue amino-terminal transport peptide (Met-Ala-Phe-Leu-Trp-Leu-Leu-Ser-Cys-Phe-Ala-Leu-Leu-Gly-Thr-Ala-Phe-Gly ), which we have previously shown to mediate the translocation of chymotrypsinogen 2 across the rough endoplasmic reticulum membrane. Following the transport peptide is a 245-residue proenzyme, which shows 82% and 80% sequence identity with bovine chymotrypsinogens A and B, respectively. Conserved among the three zymogens are 10 Cys residues that form five disulfide bonds in bovine chymotrypsinogens A and B and the residues that are required for zymogen activation, substrate binding, and catalytic activity.

CT Check Tags: Animal; Comparative Study; Human; Support, U.S. Gov't, P.H.S.
**Amino Acid Sequence**
**Base Sequence**
*Chymotrypsinogen: GE, genetics
*Cloning, Molecular
Dogs
*DNA: ME, metabolism
*Enzyme Precursors: GE, genetics
***Genes, Structural**
Nucleic Acid Hybridization
*Pancreas: EN, enzymology
***RNA, Messenger: GE, genetics**
Species Specificity

RN 89190-71-6 (prechymotrypsinogen 2); 9007-49-2 (DNA); 9035-75-0 (Chymotrypsinogen)

CN 0 (Enzyme Precursors); 0 (RNA, Messenger)

=> d all tot l108

L108 ANSWER 1 OF 2 MEDLINE
AN 2000386951 MEDLINE
DN 20316085
TI Studies on codon usage in Entamoeba histolytica.
AU Ghosh T C; Gupta S K; Majumdar S
CS Distributed Information Centre, Bose Institute, P 1/12, C.I.T. Scheme, VII M, 700 054, Calcutta, India.. tapash@boseinst.ernet.in
SO INTERNATIONAL JOURNAL FOR PARASITOLOGY, (2000 May) 30 (6) 715-22. Journal code: GSB. ISSN: 0020-7519.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-AB002796; GENBANK-AB013399; GENBANK-AB082519; GENBANK-AF013986; GENBANK-AF017993; GENBANK-AF055340; GENBANK-AF085196; GENBANK-L02417; GENBANK-L02418; GENBANK-L03534; GENBANK-L10411; GENBANK-L34567; GENBANK-L35898; GENBANK-M19871; GENBANK-M80910; GENBANK-M84155; GENBANK-M84652; GENBANK-M88600; GENBANK-M92073; GENBANK-U01051; GENBANK-U01052; GENBANK-U01053; GENBANK-U01055; GENBANK-U02529; GENBANK-U09736; GENBANK-U29270; GENBANK-U30149; GENBANK-U70560; GENBANK-U83615; GENBANK-U89655; +
EM 200010
AB Codon usage bias of Entamoeba histolytica, a protozoan parasite, was investigated using the available DNA sequence data. Entamoeba histolytica having AT rich genome, is expected to have A and/or T at the third position of codons. Overall codon usage data analysis indicates that A and/or T ending codons are strongly biased in the coding region of this organism. However, multivariate statistical analysis suggests that there

is a single major trend in codon usage variation among the genes. The genes which are supposed to be highly expressed are clustered at one end, while the majority of the putatively lowly expressed genes are clustered at the other end. The codon usage pattern is distinctly different in these two sets of genes. C ending codons are significantly higher in the putatively highly expressed genes suggesting that C ending codons are translationally **optimal** in this organism. In the putatively lowly expressed genes A and/or T ending codons are predominant, which suggests that compositional constraints are playing the major role in shaping codon usage variation among the lowly expressed genes. These results suggest that both mutational bias and translational selection are operational in the codon usage variation in this organism.

CT Check Tags: Animal; Support, Non-U.S. Gov't
***Codon**
**DNA Mutational Analysis**
DNA, Protozoan: CH, chemistry
*Entamoeba histolytica: GE, genetics
Gene Library
Molecular Sequence Data
Structure-Activity Relationship
Variation (Genetics)

CN 0 (Codon); 0 (DNA, Protozoan)

L108 ANSWER 2 OF 2 MEDLINE
AN 2000171175 MEDLINE
DN 20171175
TI Cloning and characterization of the gene encoding the highly expressed ribosomal protein l3 of the ciliated protozoan Tetrahymena thermophila. Evidence for differential codon usage in highly expressed genes.
AU Larsen L K; Andreasen P H; Dreisig H; Palm L; Nielsen H; Engberg J; Kristiansen K
CS Department of Molecular Biology, Odense University, Campusvej 55, Odense M, DK-5260, Denmark.. kong@biobase.dk
SO CELL BIOLOGY INTERNATIONAL, (1999) 23 (8) 551-60.
Journal code: BPN. ISSN: 1065-6995.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200006
EW 20000603
AB We have cloned and characterized the cDNA and the macronuclear genomic copy of the highly conserved ribosomal protein (r-protein) L3 of Tetrahymena thermophila. The r-protein L3 is encoded by a single copy gene interrupted by one intron. The organization of the promoter region exhibits features characteristic of ribosomal protein genes in Tetrahymena. The codon usage of the L3 gene is highly biased. A thorough analysis of codon usage in Tetrahymena genes revealed that genes could be categorized into two classes according to codon usage bias. Class A comprises r-protein genes and a number of other highly expressed genes. Class B comprises weakly expressed genes such as the conjugation induced CnjB and CnjC genes, but surprisingly, this class also contains abundantly expressed genes such as the genes encoding the surface antigens SerH3 and SerH1. Codon usage is slightly more restricted in class A than in class B, but both classes exhibit distinct and different codon usage biases. Class A genes preferentially use C and U in the silent third codon positions, whereas class B genes preferentially use A and U in the silent third codon positions. The analysis suggests that two different strategies have been employed for **optimization** of codon usage in the A+T-rich genome of Tetrahymena. Copyright 1999 Academic Press.

CT Check Tags: Animal; Support, Non-U.S. Gov't
Base Sequence
Cloning, Molecular
***Codon: GE, genetics**
**DNA Mutational Analysis**
Gene Expression Regulation

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      Gene Library
      Genes, Protozoan
      Introns: GE, genetics
      Molecular Sequence Data
      Mutation
      Promoter Regions (Genetics): GE, genetics
      Protozoan Proteins: GE, genetics
     *Ribosomal Proteins: GE, genetics
     *Tetrahymena thermophila: GE, genetics
CN    0 (ribosomal protein L3); 0 (Codon); 0 (Protozoan Proteins); 0 (Ribosomal
      Proteins)


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     (FILE 'HCAPLUS' ENTERED AT 13:32:47 ON 18 MAR 2001)

     FILE 'MEDLINE' ENTERED AT 13:33:18 ON 18 MAR 2001
L57       252047 S RNA+NT/CT
L58        95278 S L57/MAJ
L59        41410 S L58 AND RNA, MESSENGER+NT/CT
L60        87700 S L58 AND PY<=1998
L61        37303 S L59 AND L60
L62           50 S L61 AND GENES, SYNTHETIC+NT/CT
L63         1277 S L61 AND RECOMBINATION, GENETIC+NT/CT
L64         9336 S L61 AND GENE EXPRESSION REGULATION+NT/CT
L65        14554 S L61 AND BASE SEQUENCE+NT/CT
L66          401 S L61 AND BASE COMPOSITION+NT/CT
L67         2934 S L61 AND CODON+NT/CT
L68          628 S L61 AND INTRONS+NT/CT
L69         2919 S L61 AND G5.331.375.700./CT
L70         3505 S L61 AND GENETIC CODE+NT/CT
L71          948 S L61 AND EXONS+NT/CT
L72          492 S L61 AND (OPTIMAL? OR OPTIMIZ?)
L73         3192 S L61 AND (STABIL? OR STABL?)
L74          276 S L72 AND L62-L71
L75         2131 S L73 AND L62-L71
L76           43 S L74 AND L75
L77       143314 S RNA, MESSENGER+NT/CT
L78           34 S L77/MAJ AND L76
L79           34 S L78 AND G5./CT
L80         6319 S L18
L81         9461 S  FACTOR VIII+NT/CT
L82         9463 S L80,L81
L83           14 S L77/MAJ AND L82
L84           57 S L77 AND G5./CT AND L82
L85           12 S L84 AND L62-L76
L86           92 S L79,L83-L85
L87            4 S L86 AND (GENETIC VECTORS+NT)/CT
L88          288 S DNA MUTATIONAL ANALYSIS+NT/CT AND L77/MAJ
L89            2 S L88 AND L82
L90           92 S L86,L87,L89
L91          226 S L88 AND L62-L76
L92        31873 S SEQUENCE ANALYSIS, DNA+NT/CT
L93          493 S SEQUENCE ANALYSIS, RNA+NT/CT
L94           53 S L93 AND L77/MAJ
L95          145 S L90,L94
L96          440 S L93 NOT L95
L97          501 S L77/MAJ AND (OPTIMAL? OR OPTIMIZ?)
L98           34 S L97 AND L79
L99            1 S L97 AND L82
L100          35 S L97 AND L86
L101           2 S L97 AND L87
L102           9 S L97 AND L88
L103          35 S L97 AND L90
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L104          7 S L97 AND L91
L105         36 S L97 AND L95
L106         43 S L98-L105
L107         41 S L106 AND L60
L108          2 S L106 NOT L107

     FILE 'MEDLINE' ENTERED AT 13:55:49 ON 18 MAR 2001
L109      33918 S L77/MAJ AND PY<=1998
L110      87700 S L60,L109
L111         17 S L110 AND FURIN
L112         23 S L110 AND PACE
L113         40 S L111,L112
L114          0 S L111 AND L112
L115         99 S  HYBRIDIZATION+NT/CT AND L77/MAJ
L116         66 S L115 NOT AB/FA
L117         33 S L115 NOT L116
L118         99 S L115 AND L60,L62-L76,L82,L83-L91,L93
L119         33 S L117 AND L118
L120      10911 S CODON+NT/CT
L121       2171 S L120/MAJ AND L77/MAJ
L122       2171 S L120/MAJ AND L57/MAJ
L123       2171 S L121,L122
L124       1869 S L123 AND PY<=1998
L125         61 S L124 AND (OPTIMAL? OR OPTIMIZ?)
L126        111 S L124 AND (STABIL? OR STABL?)
L127        164 S L125,L126
L128          2 S L127 NOT AB/FA
L129        164 S L127,L128
L130          0 S L118 AND L129
L131         53 S L129 AND (SYNTH? OR BIOSYN?)
L132        119 S L129 AND RNA
L133         60 S L129 AND MRNA
L134        126 S L132,L133

=> d all tot l134


L134 ANSWER 1 OF 126  MEDLINE
AN   1998332220     MEDLINE
DN   98332220
TI   An RNA model system for investigation of pseudouridine
     stabilization of the codon-anticodon interaction in tRNALys,
     tRNAHis and tRNATyr.
AU   Davis D R; Veltri C A; Nielsen L
CS   Department of Medicinal Chemistry, University of Utah, Salt Lake City
     84112-5820, USA.. davis@adenosine.pharm.utah.edu
NC   GM55508 (NIGMS)
     RR06262 (NCRR)
     CA42014 (NCI)
SO   JOURNAL OF BIOMOLECULAR STRUCTURE AND DYNAMICS, (1998 Jun) 15
     (6) 1121-32.
     Journal code: AH2. ISSN: 0739-1102.
CY   United States
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   Priority Journals
EM   199812
EW   19981201
AB   The nucleoside conformation of pseudouridine (psi) was investigated in a
     series of RNA oligonucleotides and compared with the same
     sequences containing the parent, unmodified uridine nucleoside. 1H NMR
     spectroscopy was used to determine the glycosyl conformational preference
     in pseudouridine systems at the nucleoside level; these experiments were
     extended to trimers, and ultimately to RNA tetraloop hairpins
     that are models for the codon-anticodon interaction in tRNA. ROESY 1D and
     2D NMR experiments were used to measure the nucleoside conformational
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preference as a function of temperature. The thermodynamic **stability** of the **RNA** tetraloops was also analyzed using UV monitored Tm experiments which established that pseudouridine has a very strong **stabilizing** effect on double-stranded, base pairing interactions when the modification is located within a base-paired region. This was shown for a tetraloop hairpin model of the codon-anticodon interaction in tRNA(Tyr) which contains a psi at position 35. Pseudouridine also **stabilizes** double-stranded **RNA** when the psi modification is in a single-stranded region adjacent to a duplex region as occurs for psi at positions 38 or 39 in tRNA(Lys) and tRNA(His). These results establish that pseudouridine modification of **RNA** is a powerful and versatile mechanism for **stabilizing** local **RNA** structure in both single-stranded and double-stranded regions. Previously postulated roles for pseudouridine as a "conformational switch" are unlikely in light of the increased barrier to rotation about the glycosyl bond upon modification of uridine to pseudouridine. The Tm and NMR data show that local **RNA** stacking **stabilization** as a result of psi will **stabilize** adjacent double-stranded **RNA** regions such as the codon-anticodon interaction in tRNA.

CT Check Tags: Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.
***Anticodon**
***Codon**
*Models, Molecular
*Nucleic Acid Conformation
Protons
*Pseudouridine
***RNA, Bacterial: CH, chemistry**
***RNA, Transfer, His: CH, chemistry**
***RNA, Transfer, Lys: CH, chemistry**
***RNA, Transfer, Tyr: CH, chemistry**
Spectrophotometry, Ultraviolet
Thermodynamics
RN 1445-07-4 (Pseudouridine)
CN 0 (Anticodon); 0 (Codon); 0 (Protons); 0 (**RNA**, Bacterial); 0 (**RNA**, Transfer, His); 0 (**RNA**, Transfer, Lys); 0 (**RNA**, Transfer, Tyr)

L134 ANSWER 2 OF 126 MEDLINE
AN 1998161533 MEDLINE
DN 98161533
TI A splice-site mutation that induces exon skipping and reduction in lysyl hydroxylase **mRNA** levels but does not create a nonsense codon in Ehlers-Danlos syndrome type VI.
AU Pajunen L; Suokas M; Hautala T; Kellokumpu S; Tebbe B; Kivirikko K I; Myllyla R
CS Biocenter and Department of Medical Biochemistry, University of Oulu, Linnanmaa, Finland.
SO DNA AND CELL BIOLOGY, **(1998 Feb)** 17 (2) 117-23.
Journal code: AF9. ISSN: 1044-5498.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199805
EW 19980503
AB The type VI variant of Ehlers-Danlos syndrome (EDS) is a heritable connective tissue disorder caused by a deficiency in the activity of lysyl hydroxylase, an enzyme required for the post-translational processing of collagens. We have characterized a novel type of mutation in a young female patient with type VI EDS, in which cells possess only 12% of the lysyl hydroxylase activity that is detected in unaffected cells. The syndrome was found to be caused by a homozygous insertion of two thymidines at the 5' splice site consensus sequence of intron 9 in the lysyl hydroxylase gene. The insertion interfered with normal splicing of the primary **RNA** transcript and resulted in an inframe deletion

of the 132 nucleotides coded by exon 9 from the lysyl hydroxylase **mRNA**. In addition, the mutation caused a marked reduction in the steady-state level of the truncated **mRNA**, which was less than 15% of the level found in unaffected cells. The mutation also reduced the amount of the enzyme protein produced, which was estimated to be about 20% of that in control cells. However, the mutation did not affect the **stability** of the abnormally spliced **mRNA** nor the normal localization of the enzyme protein in the endoplasmic reticulum. According to our results, the reduction in enzymatic activity observed in this patient is caused by low levels of both lysyl hydroxylase **mRNA** and enzyme protein. The primary cellular defect associated with this mutation, therefore, appears to be at the level of nuclear **mRNA** metabolism even though the mutation did not create a premature translation termination codon.

CT Check Tags: Case Report; Female; Human; Support, Non-U.S. Gov't
***Codon, Nonsense**
DNA Mutational Analysis
Ehlers-Danlos Syndrome: EN, enzymology
*Ehlers-Danlos Syndrome: GE, genetics
*Exons
Infant, Newborn
Mutagenesis, Insertional
*Mutation
Pedigree
*Procollagen-Lysine, 2-Oxoglutarate 5-Dioxygenase: GE, genetics
Procollagen-Lysine, 2-Oxoglutarate 5-Dioxygenase: ME, metabolism
**RNA Processing, Post-Transcriptional**
***RNA Splicing: GE, genetics**
**RNA, Messenger: GE, genetics**
**RNA, Messenger: ME, metabolism**
Skin: EN, enzymology

CN EC 1.14.11.4 (Procollagen-Lysine, 2-Oxoglutarate 5-Dioxygenase); 0 (Codon, Nonsense); 0 (**RNA**, Messenger)

L134 ANSWER 3 OF 126 MEDLINE
AN 1998083113 MEDLINE
DN 98083113
TI A prokaryotic-like mode of cytoplasmic eukaryotic ribosome binding to the initiation codon during internal translation initiation of hepatitis C and classical swine fever virus **RNAs**.
AU Pestova T V; Shatsky I N; Fletcher S P; Jackson R J; Hellen C U
CS Department of Microbiology and Immunology, Morse Institute for Molecular Genetics, State University of New York Health Science Center at Brooklyn, Brooklyn, New York 11203, USA.
SO GENES AND DEVELOPMENT, **(1998 Jan 1)** 12 (1) 67-83.
Journal code: FN3. ISSN: 0890-9369.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199804
EW 19980403
AB Initiation of translation of hepatitis C virus and classical swine fever virus **mRNAs** results from internal ribosomal entry. We reconstituted internal ribosomal entry in vitro from purified translation components and monitored assembly of 48S ribosomal preinitiation complexes by toe-printing. Ribosomal subunits (40S) formed **stable** binary complexes on both **mRNAs**. The complex structure of these **RNAs** determined the correct positioning of the initiation codon in the ribosomal "P" site in binary complexes. Ribosomal binding and positioning on these **mRNAs** did not require the initiation factors eIF3, eIF4A, eIF4B, and eIF4F and translation of these **mRNAs** was not inhibited by a trans-dominant eIF4A mutant. Addition of Met-tRNAiMet, eIF2, and GTP to these binary ribosomal complexes resulted in formation of 48S preinitiation complexes. The striking similarities between this eukaryotic initiation mechanism and the

mechanism of translation initiation in prokaryotes are discussed.
CT Check Tags: Animal; Human; Support, Non-U.S. Gov't
eIF-2: ME, metabolism
eIF-2: PD, pharmacology
Base Sequence
***Codon, Initiator**
Cytoplasm: ME, metabolism
DNA Primers
Eukaryotic Cells
*Hepatitis C-Like Viruses: GE, genetics
*Hog Cholera Virus: GE, genetics
Molecular Sequence Data
Nucleic Acid Conformation
Peptide Chain Initiation
Peptide Initiation Factors: ME, metabolism
Peptide Initiation Factors: PD, pharmacology
Prokaryotic Cells
Rabbits
Ribosomal Proteins: ME, metabolism
*Ribosomes: ME, metabolism
**RNA, Transfer, Met: ME, metabolism**
***RNA, Viral: ME, metabolism**
Structure-Activity Relationship
*Translation, Genetic
CN 0 (eIF-2); 0 (eIF-3); 0 (eIF-4A); 0 (eIF-4B); 0 (eIF-4F); 0 (ribosomal protein S9); 0 (Codon, Initiator); 0 (DNA Primers); 0 (Peptide Initiation Factors); 0 (Ribosomal Proteins); 0 (**RNA**, Transfer, Met); 0 (**RNA**, Viral)

L134 ANSWER 4 OF 126 MEDLINE
AN 1998030094 MEDLINE
DN 98030094
TI Unusual effect of clusters of rare arginine (AGG) codons on the expression of human interferon alpha 1 gene in Escherichia coli.
AU Ivanov I G; Saraffova A A; Abouhaidar M G
CS Institute of Molecular Biology, Bulgaria Academy of Sciences, Sofia, Bulgaria.
SO INTERNATIONAL JOURNAL OF BIOCHEMISTRY AND CELL BIOLOGY, **(1997 Apr)** 29 (4) 659-66.
Journal code: CDK. ISSN: 1357-2725.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199802
AB The human interferon (hIFN alpha 1) gene contains 11 arginine (Arg) codons AGG or AGA, which are extremely rare for bacteria, four of which are organized in tandems. The two AGG tandems (corresponding to Arg12 Arg13 and Arg163 Arg164) are known to inhibit the translation of hIFN alpha 1 **mRNA** and therefore they are considered to be responsible for the poor expression of hIFN alpha 1 gene in bacterial cells. To study the effect of these two tandems on the expression of hIFN alpha 1 in E. coli, four new gene variants were designed to contain preferential Arg codons (CGT) substituted for the rare AGG codons in either the first, the second or both AGG tandems. We found that, whereas the yield of hIFN alpha 1 protein per cell remained unchanged, the level of hIFN alpha 1 **mRNA** decreased gradually (by a factor of two) with the consecutive substitution of the first, second and both AGG tandems. These results indicated, first, that the AGG clusters might have a **stabilizing** effect on the **mRNA**, and second, that **mRNAs** devoid of such clusters were translated at a higher rate in vivo. The protein products of the four genes (having the same amino acid sequence) showed different specific antiviral activity. The most active was the product of gene hIFN alpha 1(c) in which the second AGG tandem (corresponding to Arg163, Arg164) was preserved while the least active was the protein of gene hIFN alpha 1(d) (devoid of both AGG clusters). The role of the AGG

tandems in folding of the gene product is discussed.
CT Check Tags: Human; Support, Non-U.S. Gov't
Arginine: GE, genetics
***Codon**
*Escherichia coli: GE, genetics
*Gene Expression Regulation, Bacterial
Interferon Type I, Recombinant: BI, biosynthesis
Interferon Type I, Recombinant: GE, genetics
Interferon-alpha: BI, biosynthesis
*Interferon-alpha: GE, genetics
*Multigene Family
RN 7004-12-8 (Arginine)
CN 0 (Codon); 0 (Interferon Type I, Recombinant); 0 (Interferon-alpha)

L134 ANSWER 5 OF 126 MEDLINE
AN 1998019101 MEDLINE
DN 98019101
TI Codon **optimization** for high-level expression of human erythropoietin (EPO) in mammalian cells.
AU Kim C H; Oh Y; Lee T H
CS Biotech Research Institute, LG Chem, Taejeon, South Korea.
SO GENE, **(1997 Oct 15)** 199 (1-2) 293-301.
Journal code: FOP. ISSN: 0378-1119.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199801
EW 19980104
AB Codon bias has been observed in many species. The usage of selective codons in a given gene is positively correlated with its expression efficiency. As an experimental approach to study codon-usage effects on heterologous gene expression in mammalian cells, we designed two human erythropoietin (EPO) genes, one in which native codons were systematically substituted with codons frequently found in highly expressed human genes and the other with codons prevalent in yeast genes. Relative performances of the re-engineered EPO genes were evaluated with various combinations of promoters and signal leader sequences. Under the comparable set of combinations, mature EPO gene with human high-frequency codons gave a considerably higher level of expression than that with yeast high-frequency codons. However, the levels of EPO expression varied, depending on the alternate combinations. Since the promoters and the signal leader sequences that we used are known to be equally efficient in gene expression, we hypothesized that the varied expression levels were due to the linear sequence between the promoter and the coding gene sequence. To test this possibility, we designed the EPO gene with hybrid codon usage in which the 5'-proximal region of the EPO gene was synthesized with yeast-biased codons and the rest with human-biased codons. This codon-usage hybrid EPO gene substantially enhanced the level of EPO transcripts and proteins up to 2.9-fold and 13.8-fold, respectively, when compared to the level reached by the original counterpart. Our results suggest that the linear sequence between the promoter and the 5'-proximal region of a gene plays an important role in achieving high-level expression in mammalian cells.
CT Check Tags: Animal; Human; Support, Non-U.S. Gov't
Amino Acid Sequence
Base Sequence
Cell Line
***Codon: GE, genetics**
CHO Cells
DNA, Recombinant
Erythropoietin: BI, biosynthesis
*Erythropoietin: GE, genetics
*Gene Expression Regulation: GE, genetics
Genes, Structural: GE, genetics
Hamsters

Molecular Sequence Data
Nucleic Acid Conformation
Promoter Regions (Genetics): GE, genetics
**RNA, Messenger: BI, biosynthesis**
**RNA, Messenger: CH, chemistry**
Signal Peptides: GE, genetics
Species Specificity
RN 11096-26-7 (Erythropoietin)
CN 0 (Codon); 0 (DNA, Recombinant); 0 (**RNA**, Messenger); 0 (Signal Peptides)

L134 ANSWER 6 OF 126 MEDLINE
AN 1998009975 MEDLINE
DN 98009975
TI Rare codons are not sufficient to destabilize a reporter gene transcript in tobacco.
AU van Hoof A; Green P J
CS MSU-DOE Plant Research Laboratory, East Lansing 48824-1312, USA.
SO PLANT MOLECULAR BIOLOGY, **(1997 Oct)** 35 (3) 383-7.
Journal code: A6O. ISSN: 0167-4412.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199801
EW 19980104
AB In plants, as in other eukaryotes, most synonymous codons of the genetic-code are not used with equal frequency, but instead some codons are preferred, whereas others are rare. Circumstantial evidence led to the suggestion that rare codons have a negative influence on **mRNA stability**. To address this question experimentally, rare codons encoded by a Bacillus thuringiensis (B.t.) toxin gene (cryIA(c)) or a synthetic sequence were introduced into a phytohemagglutinin (PHA) reporter gene. In neither case was the **mRNA stability** appreciably diminished in **stably** transformed tobacco cell cultures nor was the accumulation of **mRNA** in transgenic plants affected. Thus rare codons do not appear to be sufficient to cause rapid degradation of the PHA **mRNA** and potentially other **mRNAs** in plants.
CT Check Tags: Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.
Cell Line
***Codon: GE, genetics**
*Genes, Reporter
*Phytohemagglutinins: GE, genetics
Plants, Transgenic
**RNA, Messenger: ME, metabolism**
Tobacco
*Transcription, Genetic
CN 0 (Codon); 0 (Phytohemagglutinins); 0 (**RNA**, Messenger)

L134 ANSWER 7 OF 126 MEDLINE
AN 1998004838 MEDLINE
DN 98004838
TI Codon usage bias and tRNA abundance in Drosophila.
AU Moriyama E N; Powell J R
CS Department of Ecology and Evolutionary Biology, Yale University, New Haven, CT 06520-8106, USA.. moriyama@peaplant.biology.yale.edu
SO JOURNAL OF MOLECULAR EVOLUTION, **(1997 Nov)** 45 (5) 514-23.
Journal code: J76. ISSN: 0022-2844.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199801
EW 19980104
AB Codon usage bias of 1,117 Drosophila melanogaster genes, as well as fewer

D. pseudoobscura and D. virilis genes, was examined from the perspective of relative abundance of isoaccepting tRNAs and their changes during development. We found that each amino acid contributes about equally and highly significantly to overall codon usage bias, with the exception of Asp which had very low contribution to overall bias. Asp was also the only amino acid that did not show a clear preference for one of its synonymous codons. Synonymous codon usage in Drosophila was consistent with " **optimal**" codons deduced from the isoaccepting tRNA availability. Interestingly, amino acids whose major isoaccepting tRNAs change during development did not show as strong bias as those with developmentally unchanged tRNA pools. Asp is the only amino acid for which the major isoaccepting tRNAs change between larval and adult stages. We conclude that synonymous codon usage in Drosophila is well explained by tRNA availability and is probably influenced by developmental changes in relative abundance.

CT Check Tags: Animal; Comparative Study; Support, U.S. Gov't, Non-P.H.S.
Amino Acids: GE, genetics
***Codon**
*Drosophila: GE, genetics
Evolution
Gene Expression Regulation, Developmental
Genes, Insect
Models, Genetic
***RNA, Transfer: GE, genetics**
RN **9014-25-9 (RNA, Transfer)**
CN 0 (Amino Acids); 0 (Codon)

L134 ANSWER 8 OF 126 MEDLINE
AN 97464071 MEDLINE
DN 97464071
TI Availability of a second upstream AUG can completely overcome inhibition of protein synthesis initiation engendered by **mRNA** secondary structure encompassing the start codon.
AU Satchidanandam V; Shivashankar Y
CS Centre for Genetic Engineering, Indian Institute of Science, Bangalore, India.. vijaya@cge.iisc.ernet.in
SO GENE, **(1997 Sep 1)** 196 (1-2) 231-7.
Journal code: FOP. ISSN: 0378-1119.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199801
EW 19980104
AB Secondary structure analysis of the **mRNA** from a nonproductive construct carrying the nonstructural gene 3 (NS3) of Japanese Encephalitis Virus revealed the presence of a potential 28 nucleotide long stem and loop beginning with the guanine of the initiation codon AUG that had a calculated **stabilization** energy of -13 kcal/mol (delta Gfzero). Provision of an additional AUG along with three codons upstream resulted in complete relief of inhibition. N-terminal amino acid sequence of the recombinant protein was consistent with initiation of protein synthesis having occurred from the upstream AUG. Similar levels of NS3 specific **RNA** in E. coli cells carrying the expressing and nonexpressing constructs and restoration of recombinant protein expression following deletion of segments beginning with the stem and loop confirmed the role of this structure in blocking expression at the level of translation initiation. Our approach exploits the ability of a ribosome in motion to open up downstream secondary structural elements of considerable **stability** and represents a novel and widely applicable strategy to overcome a block in translation initiation caused by **mRNA** secondary structure around the translation start site.
CT Check Tags: Support, Non-U.S. Gov't
Amino Acid Sequence
Base Sequence
***Codon, Initiator: GE, genetics**

Escherichia coli: GE, genetics
Gene Expression Regulation, Bacterial
Molecular Sequence Data
Nucleic Acid Conformation
Recombinant Proteins: BI, biosynthesis
Recombinant Proteins: GE, genetics
***RNA, Messenger: CH, chemistry**
Transcription, Genetic
Translation, Genetic
*Viral Nonstructural Proteins: BI, biosynthesis
*Viral Nonstructural Proteins: GE, genetics
CN 0 (Codon, Initiator); 0 (NS3 protein, flavivirus); 0 (Recombinant Proteins); 0 (**RNA**, Messenger); 0 (Viral Nonstructural Proteins)

L134 ANSWER 9 OF 126 MEDLINE
AN 97307849 MEDLINE
DN 97307849
TI Two genes encoding an endoglucanase and a cellulose-binding protein are clustered and co-regulated by a TTA codon in Streptomyces halstedii JM8.
AU Garda A L; Fernandez-Abalos J M; Sanchez P; Ruiz-Arribas A; Santamaria R I
CS Instituto de Microbiologia Bioquimica, Consejo Superior de Investigaciones Cientificas, (CSIC)/Universidad de Salamanca, Campus Miguel de Unamuno, Avda, Campo Charro s/n, Salamanca, Spain.
SO BIOCHEMICAL JOURNAL, **(1997 Jun 1)** 324 ( Pt 2) 403-11.
Journal code: 9YO. ISSN: 0264-6021.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Cancer Journals; Priority Journals
OS GENBANK-U51222
EM 199709
AB Streptomyces halstedii JM8 Cel2 is an endoglucanase of 28 kDa that is first produced as a protein of 42 kDa (p42) and is later processed at its C-terminus. Cel2 displays **optimal** activity towards CM-cellulose at pH6 and 50 degrees C and shows no activity against crystalline cellulose or xylan. The N-terminus of p42 shares similarity with cellulases included in family 12 of the beta-glycanases and the C-terminus shares similarity with bacterial cellulose-binding domains included in family II. This latter domain enables the precursor to bind so tightly to Avicel that it can only be eluted by boiling in 10% (w/v) SDS. Another open reading frame (ORF) situated 216 bp downstream from the p42 ORF encodes a protein of 40 kDa (p40) that does not have any clear hydrolytic activity against cellulosic or xylanosic compounds, but shows high affinity for Avicel (crystalline cellulose). The p40 protein is processed in old cultures to give a protein of 35 kDa that does not bind to Avicel. Translation of both ORFs is impaired in Streptomyces coelicolor bldA mutants, suggesting that a TTA codon situated at the fourth position of the first ORF is responsible for this regulation. S1 nuclease protection experiments demonstrate that both ORFs are co-transcribed.
CT Check Tags: Comparative Study; Support, Non-U.S. Gov't
Amino Acid Sequence
Bacterial Proteins: BI, biosynthesis
*Bacterial Proteins: GE, genetics
Base Sequence
Carrier Proteins: BI, biosynthesis
*Carrier Proteins: GE, genetics
*Cellulose: ME, metabolism
***Codon: GE, genetics**
DNA, Recombinant: GE, genetics
Enzyme Induction
*Gene Expression Regulation, Bacterial
*Genes, Structural, Bacterial: GE, genetics
Glycoside Hydrolases: BI, biosynthesis
*Glycoside Hydrolases: GE, genetics
Molecular Sequence Data
Open Reading Frames

Recombinant Fusion Proteins: ME, metabolism
**RNA, Transfer, Leu: PH, physiology**
Sequence Alignment
Sequence Homology, Amino Acid
Streptomyces: EN, enzymology
*Streptomyces: GE, genetics
Translation, Genetic
RN 9004-34-6 (Cellulose)
CN EC 3.2.1. (Glycoside Hydrolases); EC 3.2.1.- (Cel2 protein, Streptomyces); 0 (cellulose-binding protein p40); 0 (Bacterial Proteins); 0 (BldA gene product); 0 (Carrier Proteins); 0 (Codon); 0 (DNA, Recombinant); 0 (Recombinant Fusion Proteins); 0 (**RNA**, Transfer, Leu)

L134 ANSWER 10 OF 126 MEDLINE
AN 97277182 MEDLINE
DN 97277182
TI Analyses of frameshifting at UUU-pyrimidine sites.
AU Schwartz R; Curran J F
CS Department of Biology, Wake Forest University, PO Box 7325, Winston-Salem, NC 27109, USA.
NC GM52643 (NIGMS)
SO NUCLEIC ACIDS RESEARCH, **(1997 May 15)** 25 (10) 2005-11.
Journal code: O8L. ISSN: 0305-1048.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199708
EW 19970804
AB Others have recently shown that the UUU phenylalanine codon is highly frameshift-prone in the 3'(rightward) direction at pyrimidine 3'contexts. Here, several approaches are used to analyze frameshifting at such sites. The four permutations of the UUU/C (phenylalanine) and CGG/U (arginine) codon pairs were examined because they vary greatly in their expected frameshifting tendencies. Furthermore, these synonymous sites allow direct tests of the idea that codon usage can control frameshifting. Frameshifting was measured for these dicodons embedded within each of two broader contexts: the Escherichia coli prfB (RF2 gene) programmed frameshift site and a 'normal' message site. The principal difference between these contexts is that the programmed frameshift contains a purine-rich sequence upstream of the slippery site that can base pair with the 3'end of 16 S rRNA (the anti-Shine-Dalgarno) to enhance frameshifting. In both contexts frameshift frequencies are highest if the slippery tRNAPhe is capable of **stable** base pairing in the shifted reading frame. This requirement is less stringent in the RF2 context, as if the Shine-Dalgarno interaction can help **stabilize** a quasi-**stable** rephased tRNA:message complex. It was previously shown that frameshifting in RF2 occurs more frequently if the codon 3'to the slippery site is read by a rare tRNA. Consistent with that earlier work, in the RF2 context frameshifting occurs substantially more frequently if the arginine codon is CGG, which is read by a rare tRNA. In contrast, in the 'normal' context frameshifting is only slightly greater at CGG than at CGU. It is suggested that the Shine-Dalgarno-like interaction elevates frameshifting specifically during the pause prior to translation of the second codon, which makes frameshifting exquisitely sensitive to the rate of translation of that codon. In both contexts frameshifting increases in a mutant strain that fails to modify tRNA base A37, which is 3'of the anticodon. Thus, those base modifications may limit frameshifting at UUU codons. Finally, statistical analyses show that UUU Ynn dicodons are extremely rare in E.coli genes that have highly biased codon usage.
CT Check Tags: Support, U.S. Gov't, P.H.S.
Arginine: GE, genetics
Base Composition
Base Sequence
***Codon**
DNA Primers

Escherichia coli: GE, genetics
*Frameshifting, Ribosomal
Genetic Techniques
Phenylalanine: GE, genetics
Plasmids
Polymerase Chain Reaction: MT, methods
Restriction Mapping
***RNA, Transfer, Arg: GE, genetics**
***RNA, Transfer, Phe: GE, genetics**
Salmonella: GE, genetics
Translation, Genetic
Uracil
RN 3617-44-5 (Phenylalanine); 66-22-8 (Uracil); 7004-12-8 (Arginine)
CN 0 (Codon); 0 (DNA Primers); 0 (Plasmids); 0 (**RNA**, Transfer, Arg); 0 (**RNA**, Transfer, Phe)

L134 ANSWER 11 OF 126 MEDLINE
AN 97209461 MEDLINE
DN 97209461
TI Polysome-associated **mRNAs** are substrates for the nonsense-mediated **mRNA** decay pathway in Saccharomyces cerevisiae.
AU Zhang S; Welch E M; Hogan K; Brown A H; Peltz S W; Jacobson A
CS Department of Molecular Genetics, University of Medicine and Dentistry of New Jersey, Robert Wood Johnson Medical School, Piscataway 08854, USA.
NC GM48631 (NIGMS)
GM27757 (NIGMS)
SO RNA, **(1997 Mar)** 3 (3) 234-44.
Journal code: CHB. ISSN: 1355-8382.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199706
EW 19970601
AB In eukaryotic cells, premature termination of translation at nonsense codons has been implicated as the cause of a variety of posttranscriptional events, including rapid **mRNA** decay in the cytoplasm or the nucleus, altered splice site selection, and exon skipping. In the yeast Saccharomyces cerevisiae, nonsense codons promote accelerated **mRNA** decay, and we sought to determine the cellular location in which this degradation occurs. In this report, we demonstrate that six different **mRNAs**, including nonsense-containing transcripts of the LEU2, HIS4, PGK1, and CYH2 genes, and two wild-type **mRNAs** (the MAT(alpha)1 and CYH2 **mRNAs**), were **stabilized** when the translation elongation inhibitor cycloheximide was added to cellular growth media. Subsequent removal of cycloheximide resulted in resumption of translation and degradation of wild-type and nonsense-containing **mRNAs**. A significant fraction of the CYH2 pre-**mRNA** that accumulated in the presence of cycloheximide was associated with polysomes, but disappeared from that fraction when decay resumed in the absence of the drug. Moreover, the abundance of the spliced and unspliced forms of the untranslated U3 snRNA was shown to be unaffected in strains harboring mutations that **stabilize** nonsense-containing **mRNAs**. Taken together, these observations indicate that nonsense-containing **mRNAs** in yeast are degraded within the polysome compartment of the cell.
CT Check Tags: Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
***Codon, Nonsense**
Cycloheximide: PD, pharmacology
Cytoplasm: ME, metabolism
Introns
Mutagenesis
Peptide Chain Elongation
*Polyribosomes: ME, metabolism
***RNA, Fungal: ME, metabolism**

***RNA, Messenger: ME, metabolism**
**RNA, Small Nuclear: ME, metabolism**
*Saccharomyces cerevisiae: GE, genetics
Saccharomyces cerevisiae: ME, metabolism
Translation, Genetic
RN 66-81-9 (Cycloheximide)
CN 0 (Codon, Nonsense); 0 (**RNA**, Fungal); 0 (**RNA**, Messenger); 0 (**RNA**, Small Nuclear)

L134 ANSWER 12 OF 126 MEDLINE
AN 97070844 MEDLINE
DN 97070844
TI Maximizing transcription efficiency causes codon usage bias.
AU Xia X
CS Museum of Natural Science, Louisiana State University, Baton Rouge 70803, USA.. xxia@hkusua.hku.hk
SO GENETICS, **(1996 Nov)** 144 (3) 1309-20.
Journal code: FNH. ISSN: 0016-6731.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-L41354; GENBANK-Z24681; GENBANK-M12482; GENBANK-M12930
EM 199705
EW 19970502
AB The rate of protein synthesis depends on both the rate of initiation of translation and the rate of elongation of the peptide chain. The rate of initiation depends on the encountering rate between ribosomes and **mRNA**; this rate in turn depends on the concentration of ribosomes and **mRNA**. Thus, patterns of codon usage that increase transcriptional efficiency should increase **mRNA** concentration, which in turn would increase the initiation rate and the rate of protein synthesis. An **optimality** model of the transcriptional process is presented with the prediction that the most frequently used ribonucleotide at the third codon sites in **mRNA** molecules should be the same as the most abundant ribonucleotide at the third codon sites in **mRNA** molecules should be the same as the most abundant ribonucleotide in the cellular matrix where **mRNA** is transcribed. This prediction is supported by four kinds of evidence. First, A-ending codons are the most frequently used synonymous codons in mitochondria, where ATP is much more abundant than that of the three other ribonucleotides. Second, A-ending codons are more frequently used in mitochondrial genes than in nuclear genes. Third, protein genes from organisms with a high metabolic rate use more A-ending codons and have higher A content in their introns than those from organisms with a low metabolic rate.
CT Check Tags: Animal; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.
Base Sequence
***Codon**
DNA
*Mathematical Computing
*Models, Genetic
Molecular Sequence Data
*Transcription, Genetic
RN 9007-49-2 (DNA)
CN 0 (Codon)

L134 ANSWER 13 OF 126 MEDLINE
AN 97060335 MEDLINE
DN 97060335
TI Analysis of the tumorigenicity of the X gene of hepatitis B virus in a nontransformed hepatocyte cell line and the effects of cotransfection with a murine p53 mutant equivalent to human codon 249.
AU Oguey D; Dumenco L L; Pierce R H; Fausto N
CS Department of Pathology and Laboratory Medicine, School of Medicine, Brown University, Providence, RI, USA.

NC CA 23226 (NCI)
CA 35249 (NCI)
P30 CA 13943 (NCI)
+
SO HEPATOLOGY, **(1996 Nov)** 24 (5) 1024-33.
Journal code: GBZ. ISSN: 0270-9139.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199702
EW 19970204
AB Chronic infection with hepatitis B virus (HBV) is associated with the development of human hepatocellular carcinoma (HCC). One of the HBV genes, HBx, may have transforming potential, but this issue is still the subject of controversy. One of the major difficulties in addressing this question is the lack of a suitable in vitro model. We used a nontransformed, differentiated murine hepatocyte cell line (AML12) to transfect the HBx gene and examine its transforming capabilities. Because mutations of the p53 gene, in particular at codon 249, have been implicated in HCC development in geographical areas with high incidence of the tumor, we also studied the putative cooperative role in transformation between HBx and mutated p53 by cotransfecting HBx with a murine p53 mutant equivalent to human ser249 (ser246p53). Transfection with HBx plasmids containing the HBx gene under the control of two different promoters resulted in fewer colonies than in control plasmids. The toxic effect of HBx on colony formation was abolished by cotransfection with 246p53, suggesting that the inhibitory effect requires functionally intact p53. Clonal cell lines that **stably** expressed HBx messenger **RNA** (**mRNA**) (HBX
lines) were tested for their growth characteristics and their ability to grow in soft agar and form tumors in nude mice. At passages 19-27 after transfection, one of four HBx-expressing lines showed the capacity for anchorage-independent growth in soft agar and produced poorly differentiated hepatocellular carcinomas in 8 of 13 sites of injection in nude mice. HBX lines as well as clonal cell lines of cells transfected with 246p53 (246 cell lines), cotransfected with HBx and 246p53 (246x lines) or transfected with control plasmids, were analyzed by flow cytometry to determine the fraction of cells in S phase (SPF). 246 and 246X lines had similar SPFs that were approximately twofold greater than control or HBX lines. 246x lines showed morphological changes in culture such as marked cellular heterogeneity, cell crowding, and the presence of multinucleated giant cells, but their tumorigenicity was not increased compared with the HBX lines. These data show that HBx has a weak tumorigenicity in murine hepatocytes and that the addition of mutation of p53 at codon 249 to HBx expression does not increase tumorigenicity in AML12 cells.
CT Check Tags: Animal; Human; Support, U.S. Gov't, P.H.S.
Cell Line
***Codon**
Flow Cytometry
*Genes, p53
*Genes, Viral
*Hepatitis B Virus: GE, genetics
*Liver Neoplasms, Experimental: ET, etiology
Mice
Mice, Nude
Plasmids
**RNA, Messenger: AN, analysis**
*Trans-Activators: GE, genetics
*Transfection
CN 0 (hepatitis B virus X protein); 0 (Codon); 0 (Plasmids); 0 (**RNA**
, Messenger); 0 (Trans-Activators)

L134 ANSWER 14 OF 126 MEDLINE
AN 97041789 MEDLINE
DN 97041789

TI Comparative study on the effect of signal peptide codons and arginine codons on the expression of human interferon-alpha 1 gene in Escherichia coli.
AU Saraffova A; Maximova V; Ivanov I G; Abouhaidar M G
CS Institute of Molecular Biology, Bulgarian Academy of Sciences, Sofia, Bulgaria.
SO JOURNAL OF INTERFERON AND CYTOKINE RESEARCH, **(1996 Sep)** 16 (9) 745-9.
Journal code: CD4. ISSN: 1079-9907.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199704
EW 19970404
AB Human interferon-alpha 1 (HuIFN-alpha 1) gene containing signal peptide codons is poorly expressed in bacteria, and this is explained by the presence of clusters of rare (AGG) arginine codons in its structure. In this study, we have constructed a series of modified HuIFN-alpha 1 genes to study the effect of both residual signal peptide codons and clusters of AGG codons on gene expression in Escherichia coli cells. Our results showed that substitution of preferential for rare arginine codons in two clusters did not affect the yield, whereas deletion of the signal peptide codons led to a 10-fold increase in the yield of recombinant protein. To understand the mechanism of interference of gene structure on the expression of the HuIFN-alpha 1 gene in vivo, both the level and **stability** of HuIFN-alpha 1 **mRNA** were measured. The amount of HuIFN **mRNA** increased almost five times on deletion of the signal peptide codons from HuIFN-alpha 1 gene constructs (containing AGG clusters or not). The **stability** of **mRNA** obtained from all gene constructs was shown to be the same (half-life of 60 +/- 5 secs), indicating that the signal peptide codons interfere with both the efficiency of transcription of the HuIFN-alpha 1 gene and translation of its **mRNA**.
CT Check Tags: Comparative Study; Human; Support, Non-U.S. Gov't
Antiviral Agents: ME, metabolism
*Arginine: GE, genetics
***Codon**
Escherichia coli
Gene Deletion
Interferon-alpha: BI, biosynthesis
*Interferon-alpha: GE, genetics
*Multigene Family
Recombinant Proteins: BI, biosynthesis
*Signal Peptides: GE, genetics
RN 7004-12-8 (Arginine)
CN 0 (Antiviral Agents); 0 (Codon); 0 (Interferon-alpha); 0 (Recombinant Proteins); 0 (Signal Peptides)

L134 ANSWER 15 OF 126 MEDLINE
AN 97002373 MEDLINE
DN 97002373
TI **Stability** of a stem-loop involving the initiator AUG controls the efficiency of internal initiation of translation on hepatitis C virus **RNA**.
AU Honda M; Brown E A; Lemon S M
CS Department of Medicine, The University of North Carolina, Chapel Hill 27599-7030, USA.
NC RO1-AI32599 (NIAID)
T32-AI07151 (NIAID)
SO RNA, **(1996 Oct)** 2 (10) 955-68.
Journal code: CHB. ISSN: 1355-8382.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals

OS GENBANK-U22304; GENBANK-M67463
EM 199701
EW 19970104
AB The initiation of translation on the positive-sense **RNA** genome of hepatitis C virus (HCV) is directed by an internal ribosomal entry site (IRES) that occupies most of the 341-nt 5' nontranslated **RNA** (5'NTR). Previous studies indicate that this IRES differs from picornaviral IRESs in that its activity is dependent upon **RNA** sequence downstream of the initiator AUG. Here, we demonstrate that the initiator AUG of HCV is located within a stem-loop (stem-loop IV) involving nt -12 to +12 (with reference to the AUG). This structure is conserved among HCV strains, and is present in the 5'NTR of the phylogenetically distant GB virus B. Mutant, nearly genome-length **RNAs** containing nucleotide substitutions predicted to enhance the **stability** of stem-loop IV were generally deficient in cap-independent translation both in vitro and in vivo. Additional mutations that destabilize the stem-loop restored translation to normal. Thus, the **stability** of the stem-loop is strongly but inversely correlated with the efficiency of internal initiation of translation. In contrast, mutations that **stabilize** this stem-loop had comparatively little effect on translation of 5' truncated **RNAs** by scanning ribosomes, suggesting that internal initiation of translation follows binding of the 40S ribosome directly at the site of stem-loop IV. Because stem-loop IV is not required for internal entry of ribosomes but is able to regulate this process, we speculate that it may be **stabilized** by interactions with a viral protein, providing a mechanism for feedback regulation of translation, which may be important for viral persistence.
CT Check Tags: Human; Support, U.S. Gov't, P.H.S.
Antigens, Viral: AN, analysis
Base Sequence
Carcinoma, Hepatocellular
***Codon, Initiator**
Hepatitis Agents, GB: CH, chemistry
Hepatitis Agents, GB: GE, genetics
*Hepatitis C-Like Viruses: GE, genetics
Hepatitis C-Like Viruses: IM, immunology
Molecular Sequence Data
Mutation
*Nucleic Acid Conformation
*Peptide Chain Initiation: PH, physiology
Ribosomes: ME, metabolism
***RNA, Viral: CH, chemistry**
**RNA, Viral: GE, genetics**
Sequence Alignment
Sequence Homology, Nucleic Acid
Tumor Cells, Cultured
CN 0 (Antigens, Viral); 0 (Codon, Initiator); 0 (**RNA**, Viral)

L134 ANSWER 16 OF 126 MEDLINE
AN 96407840 MEDLINE
DN 96407840
TI Premature nonsense codons decrease the **stability** of phytohemagglutinin **mRNA** in a position-dependent manner.
AU van Hoof A; Green P J
CS MSU-DOE Plant Research Laboratory, Michigan State University, East Lansing 48824-1312, USA.
SO PLANT JOURNAL, **(1996 Sep)** 10 (3) 415-24.
Journal code: BRU. ISSN: 0960-7412.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199704
EW 19970402
AB Premature termination of translation has often been associated with

decreased **mRNA** accumulation in plants, but the affected step in gene expression has not been identified. To investigate this problem, the expression of wild-type and mutant alleles of the bean phytohemagglutinin (PHA) gene has been examined in tobacco cells and transgenic plants. Measurement of **mRNA** decay rates in **stably** transformed cell lines demonstrated that premature nonsense codons markedly destabilized the **mRNA**. This decreased **stability** was also reflected by decreased accumulation of transcripts containing premature nonsense codons in transgenic plants. The positional dependence of the nonsense codon effect was evaluated by introducing premature nonsense codons at different distances from the PHA AUG start codon. Transcripts with nonsense codons about 20, 40 or 60% of the way through the normal PHA coding region yielded highly unstable **mRNAs**, whereas a transcript with a nonsense codon at 80% was as **stable** as wild-type. The ability to recognize and rapidly degrade certain transcripts with early nonsense codons could provide plant cells with a means to minimize the production of wasteful and possible deleterious truncated proteins.

CT Check Tags: Support, U.S. Gov't, Non-P.H.S.
Alleles
Arabidopsis
Cell Line
**Codon, Initiator**
***Codon, Nonsense: GE, genetics**
Frameshift Mutation
*Gene Expression Regulation, Plant
*Phytohemagglutinins: GE, genetics
Phytohemagglutinins: ME, metabolism
Plants, Transgenic
**RNA, Messenger: GE, genetics**
***RNA, Messenger: ME, metabolism**
**RNA, Plant: GE, genetics**
**RNA, Plant: ME, metabolism**
Tobacco
Translation, Genetic

CN 0 (Codon, Initiator); 0 (Codon, Nonsense); 0 (Phytohemagglutinins); 0 (**RNA**, Messenger); 0 (**RNA**, Plant)

L134 ANSWER 17 OF 126 MEDLINE
AN 96332659 MEDLINE
DN 96332659
TI **mRNA** sequences influencing translation and the selection of AUG initiator codons in the yeast Saccharomyces cerevisiae.
AU Yun D F; Laz T M; Clements J M; Sherman F
CS Department of Biochemistry, University of Rochester, School of Medicine and Dentistry, New York 14642, USA.
NC T32 GM07098 (NIGMS)
R01 GM12702 (NIGMS)
SO MOLECULAR MICROBIOLOGY, **(1996 Mar)** 19 (6) 1225-39.
Journal code: MOM. ISSN: 0950-382X.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199611
AB The secondary structure and sequences influencing the expression and selection of the AUG initiator codon in the yeast Saccharomyces cerevisiae were investigated with two fused genes, which were composed of either the CYC7 or CYC1 leader regions, respectively, linked to the lacZ coding region. In addition, the strains contained the upf1-delta disruption, which **stabilized mRNAs** that had premature termination codons, resulting in wild-type levels. The following major conclusions were reached by measuring beta-galactosidase activities in yeast strains having integrated single copies of the fused genes with various alterations in the 89 and 38 nucleotide-long untranslated CYC7 and CYC1 leader regions, respectively. The leader region adjacent to the AUG

initiator codon was dispensable, but the nucleotide preceding the AUG initiator at position -3 modified the efficiency of translation by less than twofold, exhibiting an order of preference A > G > C > U. Upstream out-of-frame AUG triplets diminished initiation at the normal site, from essentially complete inhibition to approximately 50% inhibition, depending on the position of the upstream AUG triplet and on the context (-3 position nucleotides) of the two AUG triplets. In this regard, complete inhibition occurred when the upstream and downstream AUG triplets were closer together, and when the upstream and downstream AUG triplets had, respectively, **optimal** and suboptimal contexts. Thus, leaky scanning occurs in yeast, similar to its occurrence in higher eukaryotes. In contrast, termination codons between two AUG triplets causes reinitiation at the downstream AUG in higher eukaryotes, but not generally in yeast. Our results and the results of others with GCN4 **mRNA** and its derivatives indicate that reinitiation is not a general phenomenon in yeast, and that special sequences are required.

CT Check Tags: Support, U.S. Gov't, P.H.S.
Base Sequence
***Codon, Initiator: GE, genetics**
DNA, Fungal: GE, genetics
Genes, Fungal
Genetic Vectors
Molecular Sequence Data
Nucleic Acid Conformation
Plasmids: GE, genetics
**RNA, Fungal: CH, chemistry**
***RNA, Fungal: GE, genetics**
**RNA, Messenger: CH, chemistry**
***RNA, Messenger: GE, genetics**
*Saccharomyces cerevisiae: GE, genetics
Translation, Genetic

CN 0 (Codon, Initiator); 0 (DNA, Fungal); 0 (Genetic Vectors); 0 (Plasmids); 0 (**RNA**, Fungal); 0 (**RNA**, Messenger)

L134 ANSWER 18 OF 126 MEDLINE
AN 96290235 MEDLINE
DN 96290235
TI Translation of the reovirus M1 gene initiates from the first AUG codon in both infected and transfected cells.
AU Zou S; Brown E G
CS Department of Microbiology and Immunology, Faculty of Medicine, University of Ottawa, Ontario, Canada.
SO VIRUS RESEARCH, **(1996 Jan)** 40 (1) 75-89.
Journal code: X98. ISSN: 0168-1702.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199705
EW 19970504
AB Reovirus mu 2 protein can be expressed via the mouse phosphoglycerate kinase promoter to low levels in **stably** transfected L cells. To increase mu 2 expression, the terminal regions of the M1 gene cDNA constructs were modified and the effect on mu 2 expression was analyzed. The M1 gene has a single large open reading frame beginning at nucleotide 14 with another, in frame, AUG codon at nucleotide 161 reported to be used for translation initiation. Unexpectedly, deletions of the M1 5' terminal sequence upstream of the reported translation initiation codon, AUG161, resulted in loss of detection of mu 2 expression. When expression was driven by the stronger T7 promoter in the presence of recombinant vaccinia virus expressing the T7 **RNA** polymerase, constructs with the M1 5'-terminal deletion produced a smaller protein product of approximately 68 kDa, compared to approximately 73 kDa for the protein produced from the full-length M1-containing constructs consistent with the loss of 49 amino acids. The amount of shorter mu 2 product was increased by producing an improved 'Kozak' consensus sequence around the AUG codon at nucleotide 161

or by introducing an internal ribosome entry site at this location. Full-length M1 gene constructs produced a protein of the same size as the authentic mu 2 protein from virus-infected cells. It was further shown that the approximately 73 kDa product was expressed when the M1 gene was in different plasmid backgrounds and even when the M1 gene transcript was preceded by a 1 kb gene. This study demonstrated that translation of the reovirus M1 gene initiates from the first AUG codon in both infected and transfected cells.

CT Check Tags: Animal; Support, Non-U.S. Gov't
Base Sequence
Cell Line
***Codon, Initiator**
DNA Primers
Gene Expression
Mice
Molecular Sequence Data
*Orthoreovirus: GE, genetics
Plasmids
*Reovirus 3: GE, genetics
**RNA, Viral**
Sequence Deletion
*Translation, Genetic
*Viral Core Proteins: GE, genetics
3T3 Cells

CN 0 (Codon, Initiator); 0 (DNA Primers); 0 (Plasmids); 0 (**RNA, Viral**); 0 (Viral Core Proteins)

L134 ANSWER 19 OF 126 MEDLINE
AN 96282717 MEDLINE
DN 96282717
TI Upstream stimulators for recoding.
AU Larsen B; Peden J; Matsufuji S; Matsufuji T; Brady K; Maldonado R; Wills N M; Fayet O; Atkins J F; Gesteland R F
CS Department of Human Genetics, University of Utah, Salt Lake City 84112, USA.
SO BIOCHEMISTRY AND CELL BIOLOGY, **(1995 Nov-Dec)** 73 (11-12) 1123-9.
Ref: 45
Journal code: ALR. ISSN: 0829-8211.
CY Canada
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199701
EW 19970104
AB Recent progress in elucidation of 5' stimulatory elements for translational recoding is reviewed. A 5' Shine-Dalgarno sequence increases both +1 and -1 frameshift efficiency in several genes; examples cited include the E. coli prfB gene encoding release factor 2 and the dnaX gene encoding the gamma and tau subunits of DNA polymerase III holoenzyme. The spacing between the Shine-Dalgarno sequence and the shift site is critical in both the +1 and -1 frameshift cassettes; however, the **optimal** spacing is quite different in the two cases. A frameshift in a mammalian chromosomal gene, ornithine decarboxylase antizyme, has recently been reported; 5' sequences have been shown to be vital for this frameshift event. Escherichia coli bacteriophage T4 gene 60 encodes a subunit of its type II DNA topoisomerase. The mature gene 60 **mRNA** contains an internal 50 nucleotide region that appears to be bypassed during translation. A 16 amino acid domain of the nascent peptide is necessary for this bypass to occur.

CT Check Tags: Animal
Base Sequence
***Codon**
*Frameshifting, Ribosomal
Genetic Code

Mammals
Molecular Sequence Data
*Peptide Chain Termination
***RNA, Messenger: GE, genetics**
***RNA, Ribosomal: GE, genetics**
CN 0 (Codon); 0 (**RNA**, Messenger); 0 (**RNA**, Ribosomal)

L134 ANSWER 20 OF 126 MEDLINE
AN 96266423 MEDLINE
DN 96266423
TI Poliovirus neurovirulence correlates with the presence of a cryptic AUG upstream of the initiator codon.
AU Slobodskaya O R; Gmyl A P; Maslova S V; Tolskaya E A; Viktorova E G; Agol V I
CS M.P. Chumakov Institute of Poliomyelitis and Viral Encephalitides, Russian Academy of Medical Sciences, Moscow Region, Russia.
SO VIROLOGY, **(1996 Jul 1)** 221 (1) 141-50.
Journal code: XEA. ISSN: 0042-6822.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199610
AB Poliovirus mutants with extended (> 150-nt) deletions in the 5'-untranslated region between the internal ribosome entry site and the initiator codon have been selected previously (Pilipenko et al., Cell 68, 119-131, 1992; Gmyl et al., J. Virol. 67, 6309-6316, 1993). These deletions were transferred into the genome of a mouse-pathogenic poliovirus strain and found to be strongly attenuating. The deletions can be considered as covering three structural elements, a stem-loop (domain E) with a conserved cryptic AUG and two spacers, upstream and downstream of it. In an attempt to identify putative essential determinants of neurovirulence in these individual structural elements, appropriate mutants were engineered. The results demonstrated that neither of the above elements is essential for neurovirulence. The results strongly suggested that the presence of a cryptic AUG in the oligopyrimidine/AUG tandem followed, at a sufficient distance, by the initiator codon was necessary to ensure the neurovirulent phenotype of our constructs. On the other hand, the attenuated phenotype appeared to correlate with the occurrence of the initiator AUG as a moiety of the oligopyrimidine/AUG tandem. Possible mechanisms underlying these effects are discussed. Identification of the cryptic AUG as an essential determinant for neurovirulence provides a rational basis for the design of genetically **stable** attenuated poliovirus variants.
CT Check Tags: Animal; Human; Male; Support, Non-U.S. Gov't
Base Sequence
Cell Line
***Codon, Initiator**
Conserved Sequence
DNA, Ribosomal
Hela Cells
Mice
Mice, Inbred C57BL
Molecular Sequence Data
*Poliomyelitis: VI, virology
Pyrimidines
**RNA, Viral**
Sequence Deletion
Templates
Theiler Murine Encephalomyelitis Virus: GE, genetics
*Theiler Murine Encephalomyelitis Virus: PY, pathogenicity
Tumor Cells, Cultured
Virulence: GE, genetics
RN 289-95-2 (pyrimidine)
CN 0 (Codon, Initiator); 0 (DNA, Ribosomal); 0 (Pyrimidines); 0 (**RNA**, Viral)

L134 ANSWER 21 OF 126 MEDLINE
AN 96213035 MEDLINE
DN 96213035
TI Overexpression of an **mRNA** dependent on rare codons inhibits protein synthesis and cell growth.
AU Zahn K
CS Raymond and Beverly Sackler Laboratory of Molecular Genetics and Informatics, Rockefeller University, New York, New York 10021, USA.
SO JOURNAL OF BACTERIOLOGY, **(1996 May)** 178 (10) 2926-33.
Journal code: HH3. ISSN: 0021-9193.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199609
AB lambda's int gene contains an unusually high frequency of the rare arginine codons AGA and AGG, as well as dual rare Arg codons at three positions. Related work has demonstrated that Int protein expression depends on the rare AGA tRNA. Strong transcription of the int **mRNA** with a highly efficient ribosome-binding site leads to inhibition of Int protein synthesis, alteration of the overall pattern of cellular protein synthesis, and cell death. Synthesis or **stability** of int and ampicillin resistance **mRNAs** is not affected, although a portion of the untranslated int **mRNA** appears to be modified in a site-specific fashion. These phenotypes are not due to a toxic effect of the int gene product and can be largely reversed by supplementation of the AGA tRNA in cells which bear plasmids expressing the T4 AGA tRNA gene. This indicates that depletion of the rare Arg tRNA due to ribosome stalling at multiple AGA and AGG codons on the overexpressed int **mRNA** underlies all of these phenomena. It is hypothesized that int **mRNA**'s effects on protein synthesis and cell viability relate to phenomena involved in lambda phage induction and excision.
CT Check Tags: Support, Non-U.S. Gov't
*Arginine: GE, genetics
Bacteriophage lambda: GD, growth & development
Bacteriophage lambda: GE, genetics
Base Sequence
***Codon**
DNA Nucleotidyltransferases: GE, genetics
*Escherichia coli: GD, growth & development
Escherichia coli: VI, virology
Gene Expression Regulation
Molecular Sequence Data
***RNA, Messenger: BI, biosynthesis**
**RNA, Messenger: GE, genetics**
**RNA, Transfer, Arg: ME, metabolism**
***RNA, Viral: BI, biosynthesis**
**RNA, Viral: GE, genetics**
Transcription, Genetic
Transformation, Genetic
*Translation, Genetic
RN 7004-12-8 (Arginine)
CN EC 2.7.7.- (DNA Nucleotidyltransferases); EC 2.7.7.- (Integrase); 0 (Codon); 0 (**RNA**, Messenger); 0 (**RNA**, Transfer, Arg); 0 (**RNA**, Viral)

L134 ANSWER 22 OF 126 MEDLINE
AN 96211382 MEDLINE
DN 96211382
TI Accumulation of a **mRNA** decay intermediate by ribosomal pausing at a stop codon.
AU Bjornsson A; Isaksson L A
CS Department of Microbiology, Stockholm University, Sweden.
SO NUCLEIC ACIDS RESEARCH, **(1996 May 1)** 24 (9) 1753-7.
Journal code: O8L. ISSN: 0305-1048.

CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199609
AB A **RNA** fragment which is protected from degradation by ribosome pausing at a stop codon has been identified in growing Escherichia coli. The fragment is 261 nt long and corresponds to the 3'-end of the **mRNA** expressed from a semi-synthetic model gene. The 5'-end of the **RNA** fragment, denoted rpRNA (ribosomal pause **RNA**), is located 13 bases upstream of the stop codon. In vivo decay of the complete **mRNA** and accumulation of rpRNA are dependent on the nature of the stop codon and its codon context. The data indicate that the rpRNA fragment arises from interrupted decay of the S3A'**mRNA** in the 5'-->m3'direction, in connection with a ribosomal pause at the stop codon. RF-2 decoding of UGA is less efficient than RF-1 decoding of UAG in identical codon contexts, as judged from rpRNA steady-state levels. The half-life of UGA-containing rpRNAs is at least 5 min, indicating that ribosomal pausing can be a major factor in **stabilising** downstream regions of messenger **RNAs**.
CT Check Tags: Support, Non-U.S. Gov't
Base Sequence
***Codon, Terminator: GE, genetics**
*Escherichia coli: GE, genetics
Genes, Reporter: GE, genetics
Genetic Code
Half-Life
Molecular Sequence Data
*Ribosomes: PH, physiology
**RNA, Bacterial: GE, genetics**
**RNA, Bacterial: ME, metabolism**
**RNA, Messenger: GE, genetics**
***RNA, Messenger: ME, metabolism**
CN 0 (Codon, Terminator); 0 (**RNA**, Bacterial); 0 (**RNA**, Messenger)

L134 ANSWER 23 OF 126 MEDLINE
AN 96209937 MEDLINE
DN 96209937
TI Negative effect of sequential serine codons on expression of foreign genes in Escherichia coli.
AU Bula C; Wilcox K W
CS Department of Microbiology, Medical College of Wisconsin, Milwaukee, 53226, USA.
SO PROTEIN EXPRESSION AND PURIFICATION, **(1996 Feb)** 7 (1) 92-103. Journal code: BJV. ISSN: 1046-5928.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199708
AB Herpes simplex virus encodes a 1298-residue protein designated ICP4 that regulates transcription of viral genes. Structural and functional analyses of ICP4 have been facilitated by production of portions of ICP4 in Escherichia coli. We previously observed that expression of most truncated forms of ICP4 in E. coli was relatively efficient, with the exception of portions of the ICP4 gene approximately between codons 160 and 220. We have now localized the portion of ICP4 that inhibits expression to a serine-rich region from position 176 to 199. Our experimental results suggest that codons within the serine-rich domain do not induce termination of transcription, do not alter the intrinsic **stability** of **mRNA**, and do not create a proteolytically sensitive site in this portion of ICP4. Silent mutations that alter codon usage of many of the 19 serine codons in this region had no effect on expression. However, we observed that the level of protein expression was inversely proportional to the number of serine codons in this region. The results

are consistent with a model in which the serine-rich domain induces premature termination of translation. This effect is not due to any specific secondary structure in the **mRNA** or lack of sufficient seryl-tRNA synthetase. It remains to be determined whether premature termination can result from insufficient seryl-charged tRNAs. Our results suggest that foreign genes with more than 20 consecutive serine codons may be poorly expressed in E. coli.

CT Amino Acid Sequence
Amino Acyl-tRNA Ligases: ME, metabolism
Blotting, Western
*Chimeric Proteins: BI, biosynthesis
Chimeric Proteins: CH, chemistry
***Codon: GE, genetics**
Electrophoresis, Polyacrylamide Gel
*Escherichia coli: GE, genetics
Escherichia coli: ME, metabolism
*Gene Expression
Immediate-Early Proteins: BI, biosynthesis
Immediate-Early Proteins: CH, chemistry
*Immediate-Early Proteins: GE, genetics
Molecular Sequence Data
Nucleic Acid Conformation
Peptide Fragments: CH, chemistry
Peptide Fragments: GE, genetics
**RNA, Messenger: GE, genetics**
**RNA, Messenger: ME, metabolism**
**RNA, Transfer, Ser: GE, genetics**
**RNA, Transfer, Ser: ME, metabolism**
*Serine: GE, genetics
Translation, Genetic

RN 56-45-1 (Serine)

CN EC 6.1.1. (Amino Acyl-tRNA Ligases); 0 (herpes simplex virus, type 1 protein ICP4); 0 (Chimeric Proteins); 0 (Codon); 0 (Immediate-Early Proteins); 0 (Peptide Fragments); 0 (**RNA**, Messenger); 0 (**RNA**, Transfer, Ser)

L134 ANSWER 24 OF 126 MEDLINE

AN 96188843 MEDLINE

DN 96188843

TI Codon adjustment to maximise heterologous gene expression in Streptomyces lividans can lead to decreased **mRNA stability** and protein yield.

AU Lammertyn E; Van Mellaert L; Bijnens A P; Joris B; Anne J

CS Rega Institute, Katholieke Universiteit Leuven, Belgium.

SO MOLECULAR AND GENERAL GENETICS, **(1996 Feb 5)** 250 (2) 223-9.
Journal code: NGP. ISSN: 0026-8925.

CY GERMANY: Germany, Federal Republic of

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199608

AB The impact of the codon bias of the mouse tumour necrosis factor alpha (mTNF) gene cloned in Streptomyces lividans on the efficiency of expression and secretion was analysed. Minor codons occurring in the mTNF gene were therefore adapted to the codon bias of Streptomyces by site-directed mutagenesis. No improvement in mTNF yield could be detected. The **stability** of the transcript derived from the construct was shown to be more important for determining the final level of mTNF production. A strong correlation was observed between the yield of secreted biologically active mTNF and the amount of mTNF **mRNA** present in the cells.

CT Check Tags: Support, Non-U.S. Gov't
alpha-Amylase: GE, genetics
alpha-Amylase: ME, metabolism
Algorithms
Base Sequence

Blotting, Northern
Cloning, Molecular
***Codon: GE, genetics**
**Codon, Initiator: GE, genetics**
DNA Primers: CH, chemistry
*Gene Expression
Molecular Sequence Data
Mutagenesis, Site-Directed
Nucleic Acid Conformation
Promoter Regions (Genetics): GE, genetics
Recombinant Fusion Proteins: BI, biosynthesis
Recombinant Fusion Proteins: GE, genetics
**RNA, Messenger: BI, biosynthesis**
**RNA, Messenger: GE, genetics**
***RNA, Messenger: ME, metabolism**
Signal Peptides: GE, genetics
Software
*Streptomyces: GE, genetics
Tumor Necrosis Factor: BI, biosynthesis
*Tumor Necrosis Factor: GE, genetics
Tumor Necrosis Factor: SE, secretion
CN EC 3.2.1.1 (alpha-Amylase); 0 (Codon); 0 (Codon, Initiator); 0 (DNA Primers); 0 (Recombinant Fusion Proteins); 0 (**RNA**, Messenger); 0 (Signal Peptides); 0 (Tumor Necrosis Factor)

L134 ANSWER 25 OF 126 MEDLINE
AN 96135234 MEDLINE
DN 96135234
TI Translation of Sindbis virus **mRNA**: analysis of sequences downstream of the initiating AUG codon that enhance translation.
AU Frolov I; Schlesinger S
CS Department of Molecular Microbiology, Washington University, School of Medicine, St. Louis, Missouri 63110-1093, USA.
NC AI11377 (NIAID)
SO JOURNAL OF VIROLOGY, **(1996 Feb)** 70 (2) 1182-90.
Journal code: KCV. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199604
AB Alphaviruses, particularly Sinbis virus and Semliki Forest virus, are proving to be useful vectors for the expression of heterologous genes. In infected cells, these self-replicating vectors (replicons) transcribe a subgenomic **mRNA** that codes for a heterologous protein instead of the structural proteins. We reported recently that translation of the reporter gene lacZ is enhanced 10-fold when the coding sequences of this gene are fused downstream of and in frame with the 5' half of the capsid gene (I. Frolov and S. Schlesinger, J. Virol. 68:8111-8117, 1994). The enhancing sequences, located downstream of the AUG codon that initiates translation of the capsid protein, have a predicted hairpin structure. We have mutated this region by making changes in the codons which do not affect the protein sequence but should destabilize the putative hairpin structure. These changes caused a decrease in the accumulation of the capsid-beta-galactosidase fusion protein. When these alterations were inserted into the capsid gene in the context of the intact Sindbis virus genome, they led to a decrease in the rate of virus formation but did not affect the final yield. We also altered the original sequence to one that has 12 contiguous G.C base pairs and should form a **stable** hairpin. The new sequence was essentially as effective as the original had been in enhancement of translation and in the rate of virus formation. The position of the predicted hairpin structure is important for its function; an insertion of 9 nucleotides or a deletion of 9 nucleotides decreased the level of translation. The insertion of a hairpin structure at a particular location downstream of the initiating AUG appears to be a way that alphaviruses have evolved to enhance translation of their **mRNA**,

and, as a consequence, they produce high levels of the structural proteins which are needed for virus assembly. This high level of translation requires an intracellular environment in which host cell protein synthesis is inhibited.

CT Check Tags: Support, U.S. Gov't, P.H.S.
Amino Acid Sequence
Base Sequence
Binding Sites
Capsid: BI, biosynthesis
Capsid: GE, genetics
***Codon, Initiator**
Down-Regulation (Physiology)
DNA, Viral
Molecular Sequence Data
Nucleic Acid Conformation
Point Mutation
**RNA, Messenger**
***RNA, Viral: GE, genetics**
Sindbis Virus: GD, growth & development
*Sindbis Virus: GE, genetics
Structure-Activity Relationship
*Translation, Genetic
Trinucleotide Repeats
Virus Assembly

CN 0 (Capsid); 0 (Codon, Initiator); 0 (DNA, Viral); 0 (**RNA**, Messenger); 0 (**RNA**, Viral)

L134 ANSWER 26 OF 126 MEDLINE
AN 96105379 MEDLINE
DN 96105379
TI Kinetics of translation of gamma B crystallin and its circularly permutated variant in an in vitro cell-free system: possible relations to codon distribution and protein folding.
AU Komar A A; Jaenicke R
CS Institut fur Biophysik und Physikalische Biochemie, Universitat Regensburg, Germany.
SO FEBS LETTERS, **(1995 Dec 4)** 376 (3) 195-8.
Journal code: EUH. ISSN: 0014-5793.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199603
AB Analysis of nascent gamma B-crystallin peptides accumulating during in vitro translation in a rabbit reticulocyte lysate cell-free system was carried out. As a consequence of the irregular distribution of rare codons along the polypeptide chain of gamma B-crystallin, translation of the two-domain protein is a non-uniform process characterized by specific pauses. One of the major delays occurs during the translation of the connecting peptide between the domains. Comparing the kinetics of translation of natural gamma B-crystallin and its circularly permutated variant (with the order of the N- and C-terminal domains exchanged) reveals that the natural N-terminal domain is translated faster than the C-terminal one. Since the N-terminal domain in natural gamma B-crystallin is known to be more **stable** and to fold faster than the C-terminal one [E.-M. Mayr et al. (1994) J. Mol. Biol. 235, 84-88], the present data suggest that the translation rates are **optimized** to tune the synthesis and folding of the nascent polypeptide chain. In this connection, the pause in the linker region between the domains provides a delay allowing the correct folding of the N-terminal domain and its subsequent assistance in the **stabilization** of the C-terminal one.

CT Check Tags: Animal; Support, Non-U.S. Gov't
Cattle
Cell-Free System
***Codon**

*Crystallins: CH, chemistry
Crystallins: GE, genetics
Kinetics
Protein Folding
Rabbits
Reticulocytes
**RNA, Messenger: GE, genetics**
*Translation, Genetic
CN 0 (Codon); 0 (Crystallins); 0 (**RNA**, Messenger)

L134 ANSWER 27 OF 126 MEDLINE
AN 96096738 MEDLINE
DN 96096738
TI Glycine reductase of Clostridium litorale. Cloning, sequencing, and molecular analysis of the grdAB operon that contains two in-frame TGA codons for selenium incorporation.
AU Kreimer S; Andreesen J R
CS Institut fur Mikrobiologie, Georg-August-Universitat Gottingen, Germany.
SO EUROPEAN JOURNAL OF BIOCHEMISTRY, **(1995 Nov 15)** 234 (1) 192-9.
Journal code: EMZ. ISSN: 0014-2956.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-U24268
EM 199604
AB A 2.8-kb HindIII fragment, containing three open reading frames, has been cloned and sequenced from Clostridium litorale. The first gene grdA encoded the selenocysteine-containing protein PA of the glycine reductase complex, a protein of 159 amino acids with a deduced molecular mass of 16.7 kDa. The second gene (grdB) encoded the 47-kDa subunit of the substrate-specific selenoprotein PB glycine that is composed of 437 amino acids. The third gene contained the 5'-region of the gene for thioredoxin reductase, trxB. All gene products shared high similarity with the corresponding proteins from Eubacterium acidaminophilum. In both genes grdA and grdB, the opal termination codon (TGA) was found inframe, indicating the presence of selenocysteine in both polypeptides. Northern-blot analysis showed that grdA and grdB are organized as one operon. Unlike Escherichia coli, no **stable** secondary structures of the corresponding **mRNA** were found immediately downstream of the UGA codons to direct an insertion of selenocysteine into the grdA and grdB transcripts of C. litorale. Instead, a secondary structure was identified in the 3'-untranslated region of grdB.
CT *Amino Acid Oxidoreductases: GE, genetics
Amino Acid Oxidoreductases: ME, metabolism
Amino Acid Sequence
*Bacterial Proteins: GE, genetics
Base Sequence
Blotting, Northern
Cloning, Molecular
*Clostridium: EN, enzymology
***Codon**
DNA, Bacterial
Molecular Sequence Data
*Multienzyme Complexes: GE, genetics
Multienzyme Complexes: ME, metabolism
Nucleic Acid Conformation
*Operon
**RNA, Messenger: CH, chemistry**
**RNA, Messenger: GE, genetics**
*Selenium: ME, metabolism
Sequence Homology, Amino Acid
RN 7782-49-2 (Selenium)
CN EC 1.4. (Amino Acid Oxidoreductases); EC 1.4.1.- (glycine reductase); 0 (grdA protein); 0 (selenoprotein A); 0 (selenoprotein B); 0 (Bacterial Proteins); 0 (Codon); 0 (DNA, Bacterial); 0 (Multienzyme Complexes); 0 (

**RNA**, Messenger)

L134 ANSWER 28 OF 126 MEDLINE
AN 95303110 MEDLINE
DN 95303110
TI [Analysis of stationary kinetics of translation elongation within the framework of the stereospecific **stabilization** hypothesis of codon- anticodon complexes in a ribosome. II. Kinetic schemes in the presence of protein elongation factors and GTP].
Analiz statsionarnoi kinetiki elongatsii transliatsii v ramkakh gipotezy o stereospetsificheskoi **stabilizatsii** kodon-antikodonovykh kompleksov na ribosome. II. Kineticheskie skhemy v prisutstvii belkovykh faktorov elongatsii i GTP.
AU Saifullin S R; Potapov A P
SO MOLEKULIARNAIA BIOLOGIIA, **(1995 Mar-Apr)** 29 (2) 434-45.
Journal code: NGX. ISSN: 0026-8984.
CY RUSSIA: Russian Federation
DT Journal; Article; (JOURNAL ARTICLE)
LA Russian
FS Priority Journals
EM 199509
AB Kinetics of the factor-dependent polypeptide elongation is theoretically studied in context of stereospecific **stabilization** of the codon-anticodon complexes at a ribosome. Kinetic schemes for the different ribosome isomerization stages are examined. The dependence of steady-state elongation rate on elongation factor concentration for each of the schemes is unique, allowing to identify isomerization stages experimentally.
CT ***Anticodon**
***Codon**
English Abstract
*Guanosine Triphosphate: CH, chemistry
Isomerism
Kinetics
*Peptide Elongation Factors: CH, chemistry
*Ribosomes: CH, chemistry
**RNA, Transfer, Amino Acyl: CH, chemistry**
*Translation, Genetic
RN 86-01-1 (Guanosine Triphosphate)
CN 0 (Anticodon); 0 (Codon); 0 (Peptide Elongation Factors); 0 (**RNA**, Transfer, Amino Acyl)

L134 ANSWER 29 OF 126 MEDLINE
AN 95303109 MEDLINE
DN 95303109
TI [Analysis of stationary kinetics of translation elongation within the framework stereospecific **stabilization** hypothesis of codon-anticodon complexes in a ribosome. I. Kinetic schemes of factorless elongation].
Analiz statsionarnoi kinetiki elongatsii transliatsii v ramkakh gipotezy o stereospetsificheskoi **stabilizatsii** kodon-antikodonovykh kompleksov na ribosomes. I. Kineticheskie skhemy besfaktornoi elongatsii.
AU Saifullin S R; Potapov A P
SO MOLEKULIARNAIA BIOLOGIIA, **(1995 Mar-Apr)** 29 (2) 421-33.
Journal code: NGX. ISSN: 0026-8984.
CY RUSSIA: Russian Federation
DT Journal; Article; (JOURNAL ARTICLE)
LA Russian
FS Priority Journals
EM 199509
AB Dependences of steady-state rates of polypeptide elongation on concentrations of substrate (aminoacyl-tRNA) and product (deacylated tRNA) in the absence of elongation factors and GTP are theoretically analyzed in context of stereospecific **stabilization** of the codon-anticodon complexes at a ribosome. General kinetic scheme and different ribosome isomerization stages are examined. The effect of isomerization stage allows to identify reaction stage experimentally. Regulation of the direct

reaction by product and regulation of the reverse reaction by substrate are possible. Under certain conditions elongation system may show kinetic cooperativity.

CT ***Anticodon**
Binding Sites
***Codon**
English Abstract
Isomerism
Kinetics
*Ribosomes: CH, chemistry
**RNA, Transfer, Amino Acyl: CH, chemistry**
*Translation, Genetic

CN 0 (Anticodon); 0 (Codon); 0 (**RNA**, Transfer, Amino Acyl)

L134 ANSWER 30 OF 126 MEDLINE
AN 95189082 MEDLINE
DN 95189082
TI Identification and characterization of genes that are required for the accelerated degradation of **mRNAs** containing a premature translational termination codon.
AU Cui Y; Hagan K W; Zhang S; Peltz S W
CS Department of Molecular Genetics and Microbiology, Robert Wood Johnson Medical School, University of Medicine, Piscataway, New Jersey.
NC GM48631-01 (NIGMS)
SO GENES AND DEVELOPMENT, **(1995 Feb 15)** 9 (4) 423-36.
Journal code: FN3. ISSN: 0890-9369.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-U12137
EM 199506
AB In both prokaryotes and eukaryotes nonsense mutations in a gene can enhance the decay rate of the **mRNA** transcribed from the gene, a phenomenon described as nonsense-mediated **mRNA** decay. In yeast, the products of the UPF1 and UPF3 genes are required for this decay pathway, and in this report we focus on the identification and characterization of additional factors required for rapid decay of nonsense-containing **mRNAs**. We present evidence that the product of the UPF2 gene is a new factor involved in this decay pathway. Mutation of the UPF2 gene or deletion of it from the chromosome resulted in **stabilization** of nonsense-containing **mRNAs**, whereas the decay of wild-type transcripts was not affected. The UPF2 gene was isolated, and its transcript was characterized. Our results demonstrate that the UPF2 gene encodes a putative 126.7-kD protein with an acidic region at its carboxyl terminus (-D-E)n found in many nucleolar and transcriptional activator proteins. The UPF2 transcript is 3600 nucleotides in length and contains an intron near its 5' end. The UPF2 gene is dispensable for vegetative growth, but upf2 delta strains were found to be more sensitive to the translational elongation inhibitor cycloheximide than UPF2+. A genetic analysis of other alleles proposed to be involved in nonsense-mediated **mRNA** decay revealed that the UPF2 gene is allelic to the previously identified sua1 allele, a suppressor of an out-of-frame ATG insertion shown previously to reduce translational initiation from the normal ATG of the CYC1 gene. In addition, we demonstrate that another suppressor of this cyc1 mutation, sua6, is allelic to upf3, a previously identified lesion involved in nonsense-mediated **mRNA** decay.

CT Check Tags: Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Alleles
Amino Acid Sequence
Base Sequence
***Codon, Terminator**
Cycloheximide: PD, pharmacology
*Fungal Proteins: GE, genetics
Fungal Proteins: ME, metabolism

*Genes, Fungal: GE, genetics
Genetic Complementation Test
Molecular Sequence Data
Mutation
**RNA, Fungal: GE, genetics**
**RNA, Fungal: ME, metabolism**
**RNA, Messenger: GE, genetics**
***RNA, Messenger: ME, metabolism**
Sequence Analysis, DNA
Suppression, Genetic
*Trans-Activators: GE, genetics
Trans-Activators: ME, metabolism
Translation, Genetic
Yeasts: DE, drug effects
*Yeasts: GE, genetics
RN 66-81-9 (Cycloheximide)
CN 0 (Codon, Terminator); 0 (Fungal Proteins); 0 (NMD2 protein); 0 (**RNA**, Fungal); 0 (**RNA**, Messenger); 0 (Trans-Activators)
GEN UPF2

L134 ANSWER 31 OF 126 MEDLINE
AN 95147270 MEDLINE
DN 95147270
TI Consecutive low-usage leucine codons block translation only when near the 5' end of a message in Escherichia coli.
AU Goldman E; Rosenberg A H; Zubay G; Studier F W
CS Department of Microbiology & Molecular Genetics, New Jersey Medical School-UMDNJ, Newark 07103..
NC GM27711 (NIGMS)
SO JOURNAL OF MOLECULAR BIOLOGY, **(1995 Feb 3)** 245 (5) 467-73.
Journal code: J6V. ISSN: 0022-2836.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199505
AB Insertion of nine consecutive low-usage CUA leucine codons after codon 13 of a 313-codon test **mRNA** strongly inhibited its translation without apparent effect on translation of other **mRNAs** containing CUA codons. In contrast, nine consecutive high-usage CUG leucine codons at the same position had no apparent effect, and neither low- nor high-usage codons affected translation when inserted after codon 223 or 307. Additional experiments indicated that the strong positional effect of the low-usage codons could not be accounted for by differences in **stability** of the **mRNAs** or in stringency of selection of the correct tRNA. The positional effect could be explained if translation complexes are less **stable** near the beginning of a message: slow translation through low-usage codons early in the message may allow most translation complexes to dissociate before they read through.
CT Check Tags: Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.
Blotting, Northern
***Codon**
*Escherichia coli: GE, genetics
*Leucine: GE, genetics
Ribosomes
**RNA, Messenger: CH, chemistry**
**RNA, Messenger: GE, genetics**
*Translation, Genetic
RN 7005-03-0 (Leucine)
CN 0 (Codon); 0 (**RNA**, Messenger)

L134 ANSWER 32 OF 126 MEDLINE
AN 95115140 MEDLINE
DN 95115140
TI Attenuation of Theiler's murine encephalomyelitis virus by modifications

of the oligopyrimidine/AUG tandem, a host-dependent translational cis element.
AU Pilipenko E V; Gmyl A P; Maslova S V; Khitrina E V; Agol V I
CS Institute of Poliomyelitis and Viral Encephalitides, Russian Academy of Medical Sciences, Moscow Region.
SO JOURNAL OF VIROLOGY, **(1995 Feb)** 69 (2) 864-70.
Journal code: KCV. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199504
AB A set of Theiler's murine encephalomyelitis virus mutants with engineered alterations in the conserved oligopyrimidine/AUG tandem (E. V. Pilipenko, A. P. Gmyl, S. V. Maslova, G. A. Belov, A. N. Sinyakov, M. Huang, T. D. K. Brown, and V. I. Agol, J. Mol. Biol. 241:398-414, 1994) were assayed for their growth potential in BHK-21 cells (as reflected in plaque size) and for neurovirulence upon intracerebral inoculation of mice. Tandem-destroying mutations, which included substitutions in the oligopyrimidine moiety and extended insertions into the oligopyrimidine/AUG spacer, exerted relatively little effect on the plaque size but ensured a high level of attenuation. The attenuated mutants exhibited remarkable genetic **stability** upon growth in BHK-21 cells. However, the brains of rare animals that developed symptoms after the inoculation with high doses of these mutants invariably contained pseudorevertants with the oligopyrimidine/AUG tandem restored by diverse deletions or an AUG-generating point mutation. The AUG moiety of the tandem in the revertant genomes was represented by either a cryptic codon or initiator codon. The results demonstrate that the tandem, while dispensable for the Theiler's murine encephalomyelitis virus growth in BHK-21 cells, is essential for neurovirulence in mice. Thus, the oligopyrimidine/AUG tandem is a host-dependent cis-acting control element that may be essential for virus replication under certain conditions. The functional activity of the tandem was retained when its oligopyrimidine or AUG moieties were made double stranded. A possible role of the tandem in the cap-independent internal initiation of translation on the picornavirus **RNA** templates is discussed.
CT Check Tags: Animal; Support, Non-U.S. Gov't
Base Sequence
Brain: VI, virology
Cell Line
***Codon**
*Genes, Regulator
Genome, Viral
Hamsters
Molecular Sequence Data
*Theiler Murine Encephalomyelitis Virus: GE, genetics
*Theiler Murine Encephalomyelitis Virus: PY, pathogenicity
*Translation, Genetic
Virulence
CN 0 (Codon)

L134 ANSWER 33 OF 126 MEDLINE
AN 95098611 MEDLINE
DN 95098611
TI Determination of the **optimal** aligned spacing between the Shine-Dalgarno sequence and the translation initiation codon of Escherichia coli **mRNAs**.
AU Chen H; Bjerknes M; Kumar R; Jay E
CS Department of Chemistry, University of New Brunswick, Fredericton, Canada.
SO NUCLEIC ACIDS RESEARCH, **(1994 Nov 25)** 22 (23) 4953-7.
Journal code: O8L. ISSN: 0305-1048.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals

EM 199503
AB The prokaryotic **mRNA** ribosome binding site (RBS) usually contains part or all of a polypurine domain UAAGGAGGU known as the Shine-Dalgarno (SD) sequence found just 5' to the translation initiation codon. It is now clear that the SD sequence is important for identification of the translation initiation site on the **mRNA** by the ribosome, and that as a result, the spacing between the SD and the initiation codon strongly affects translational efficiency (1). It is not as clear, however, whether there is a unique **optimal** spacing. Complications involving the definition of the spacing as well as secondary structures have obscured matters. We thus undertook a systematic study by inserting two series of synthetic RBSs of varying spacing and SD sequence into a plasmid vector containing the chloramphenicol acetyltransferase gene. Care was taken not to introduce any secondary structure. Measurements of protein expression demonstrated an **optimal** aligned spacing of 5 nt for both series. Since aligned spacing corresponds naturally to the spacing between the 3'-end of the 16S rRNA and the P-site, we conclude that there is a unique **optimal** aligned SD-AUG spacing in the absence of other complicating issues.
CT Check Tags: Support, Non-U.S. Gov't
Base Sequence
Binding Sites
Chloramphenicol O-Acetyltransferase: GE, genetics
***Codon, Initiator: GE, genetics**
*Escherichia coli: GE, genetics
Genes, Reporter: GE, genetics
Molecular Sequence Data
Polydeoxyribonucleotides: CS, chemical synthesis
Ribosomes
***RNA, Bacterial: GE, genetics**
**RNA, Bacterial: ME, metabolism**
***RNA, Messenger: GE, genetics**
**RNA, Messenger: ME, metabolism**
***RNA, Ribosomal, 16S: ME, metabolism**
Translation, Genetic: GE, genetics
CN EC 2.3.1.28 (Chloramphenicol O-Acetyltransferase); 0 (Codon, Initiator); 0 (Polydeoxyribonucleotides); 0 (**RNA**, Bacterial); 0 (**RNA**, Messenger); 0 (**RNA**, Ribosomal, 16S)

L134 ANSWER 34 OF 126 MEDLINE
AN 95095049 MEDLINE
DN 95095049
TI Selection intensity for codon bias.
AU Hartl D L; Moriyama E N; Sawyer S A
CS Department of Organismic and Evolutionary Biology, Harvard University, Cambridge, Massachusetts 02138..
NC GM-40322 (NIGMS)
GM-44889 (NIGMS)
SO GENETICS, **(1994 Sep)** 138 (1) 227-34.
Journal code: FNH. ISSN: 0016-6731.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199503
AB The patterns of nonrandom usage of synonymous codons (codon bias) in enteric bacteria were analyzed. Poisson random field (PRF) theory was used to derive the expected distribution of frequencies of nucleotides differing from the ancestral state at aligned sites in a set of DNA sequences. This distribution was applied to synonymous nucleotide polymorphisms and amino acid polymorphisms in the gnd and putP genes of Escherichia coli. For the gnd gene, the average intensity of selection against disfavored synonymous codons was estimated as approximately 7.3 x 10(-9); this value is significantly smaller than the estimated selection intensity against selectively disfavored amino acids in observed polymorphisms (2.0 x 10(-8)), but it is approximately of the same order of

magnitude. The selection coefficients for **optimal** synonymous codons estimated from PRF theory were consistent with independent estimates based on codon usage for threonine and glycine. Across 118 genes in E. coli and Salmonella typhimurium, the distribution of estimated selection coefficients, expressed as multiples of the effective population size, has a mean and standard deviation of 0.5 +/- 0.4. No significant differences were found in the degree of codon bias between conserved positions and replacement positions, suggesting that translational misincorporation is not an important selective constraint among synonymous polymorphic codons in enteric bacteria. However, across the first 100 codons of the genes, conserved amino acids with identical codons have significantly greater codon bias than that of either synonymous or nonidentical codons, suggesting that there are unique selective constraints, perhaps including **mRNA** secondary structures, in this part of the coding region.

CT Check Tags: Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.
***Codon: GE, genetics**
DNA, Bacterial: GE, genetics
Escherichia coli: GE, genetics
Genes, Bacterial
*Models, Genetic
Poisson Distribution
Polymorphism (Genetics)
Salmonella typhimurium: GE, genetics
*Selection (Genetics)
CN 0 (Codon); 0 (DNA, Bacterial)

L134 ANSWER 35 OF 126 MEDLINE
AN 95046889 MEDLINE
DN 95046889
TI Nonsense-mediated **mRNA** decay in Xenopus oocytes and embryos.
AU Whitfield T T; Sharpe C R; Wylie C C
CS Wellcome/CRC Institute, Cambridge, United Kingdom..
SO DEVELOPMENTAL BIOLOGY, **(1994 Oct)** 165 (2) 731-4.
Journal code: E7T. ISSN: 0012-1606.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199502
AB Mutant **mRNAs** carrying a premature stop codon have a reduced half-life in the cells of many species, probably due to the presence of "surveillance" pathways, which selectively target such **mRNAs** for degradation. It is reported here that this phenomenon may also occur in Xenopus. In vitro-synthesised transcripts encoding a Xenopus POU-domain protein, XLPOU-60, are **stable** after injection into the oocyte and embryo. However, introduction of a premature stop codon into these transcripts results in their rapid degradation following injection. In contrast, mutant transcripts with additional or deleted codons but retaining a correct reading frame are **stable**. These results suggest that **RNA stability** should be considered when designing control **mRNAs** for Xenopus injection experiments.
CT Check Tags: Animal; Support, Non-U.S. Gov't
Base Sequence
***Codon, Nonsense**
*Gene Expression Regulation, Developmental
Molecular Sequence Data
Oligodeoxyribonucleotides: CH, chemistry
Oocytes: ME, metabolism
Peptide Chain Termination
***RNA, Messenger: ME, metabolism**
*Xenopus laevis: EM, embryology
CN 0 (Codon, Nonsense); 0 (Oligodeoxyribonucleotides); 0 (**RNA,** Messenger)

L134 ANSWER 36 OF 126 MEDLINE

AN 94290935 MEDLINE
DN 94290935
TI [**Stability** of messenger **RNA** of Escherichia coli ompA is affected by the use of synonymous codon].
La **stabilite** de l'ARN messager d'ompA d'Escherichia coli est affectee par l'utilisation de codons synonymes.
AU Deana A; Reiss C
CS Institut Jacques Monod, CNRS-Universite Paris VII, France..
SO COMPTES RENDUS DE L ACADEMIE DES SCIENCES. SERIE III, SCIENCES DE LA VIE, **(1993 Jul)** 316 (7) 628-32.
Journal code: CA1. ISSN: 0764-4469.
CY France
DT Journal; Article; (JOURNAL ARTICLE)
LA French
FS Priority Journals
EM 199410
AB The ompA gene of E. coli was silently mutated by the substitution of nine codons located towards the end of the gene, by synonymous codons expected to be translated more slowly. At 37 degrees C in vivo the life-time of the ompA messenger **RNA** (**mRNA**) is reduced from 4.5 min (w.t.) to 3.8 min (silent mutant). The amount of **mRNA** of the silent mutant is only 30% of that observed for the w.t. gene. These variations are thought to be due to the uncoupling of transcription from translation, and a lesser protection of the **mRNA** towards RNase digestion by ribosomes, resulting from a lesser density of the ribosome traffic on the mutated polysome.
CT Blotting, Northern
***Codon: GE, genetics**
**Codon: ME, metabolism**
**Drug Stability**
English Abstract
*Escherichia coli: GE, genetics
*Genes, Bacterial: GE, genetics
***RNA, Messenger: GE, genetics**
**RNA, Messenger: ME, metabolism**
Translation, Genetic
CN 0 (Codon); 0 (**RNA**, Messenger)

L134 ANSWER 37 OF 126 MEDLINE
AN 94195303 MEDLINE
DN 94195303
TI [Interaction of deacylated phenylalanyl tRNA from yeasts with Escherichia coli ribosomes. The role of the modified nucleotide in codon-anticodon interaction].
Vzaimodeistvie deatsilirovannoi fenilalaninovoi tRNK iz drozhzhei s ribosomami Escherichia coli. Rol' modifitsirovannogo nukleotida v kodon-antikodonovom vazimodeistvii.
AU Katunin V I; Soboleva N G; Makhno V I; Sedel'nikova E A; Zhenodarova S M; Kirillov S V
SO MOLEKULIARNAIA BIOLOGIIA, **(1994 Jan-Feb)** 28 (1) 66-75.
Journal code: NGX. ISSN: 0026-8984.
CY RUSSIA: Russian Federation
DT Journal; Article; (JOURNAL ARTICLE)
LA Russian
FS Priority Journals
EM 199407
AB The method of anticodon loop replacement has been used to make derivatives of yeast tRNA(Phe)GmAAY with the substitution at the 37 position (tRNA(Phe)GAAA), and at both the anticodon (tRNA(Phe)GCAG) and the 37 position. A quantitative study of the interaction of various types of yeast deacylated tRNA: tRNA(Phe)GmAAY, tRNA(Phe)GAAA, tRNA(Phe)GCAG, and tRNA(Phe)-Y with the P site of the 70S ribosome.poly(U) complex was carried out at different Mg2+ concentrations and temperatures. The replacement of the Y base on the nonmodified adenosine decreases the interaction enthalpy from 39 to 24 kcal/mole, whereas the complete removal of the Y base reduces the interaction enthalpy to 16 kcal/mole. The

replacement of the second letter of the anticodon (A) with cytosine leads to a drop in the enthalpy to 6 kcal/mole, which is typical of tRNA interaction with the P site in the absence of poly(U). In the absence of poly(U) the affinity of tRNA(Phe)-Y for the P site of the 70S ribosome is 5 times lower than the affinity of tRNA(Phe)GmAAY and tRNA(Phe)GCAG. Thus, in the ribosome the modified nucleotide not only **stabilizes** the codon-anticodon interaction owing to the stacking interaction with the stack of codon-anticodon bases, but also lowers the free energy of binding as a result of the interaction of the modified nucleotide itself with the hydrophobic center of the P site on the ribosome.

CT Acylation
***Anticodon**
***Codon**
English Abstract
Escherichia coli: GE, genetics
Escherichia coli: ME, metabolism
Nucleotides: CH, chemistry
*Nucleotides: ME, metabolism
*Ribosomes: ME, metabolism
***RNA, Transfer, Phe: ME, metabolism**
*Saccharomyces cerevisiae: GE, genetics
Thermodynamics

CN 0 (Anticodon); 0 (Codon); 0 (Nucleotides); 0 (**RNA**, Transfer, Phe)

L134 ANSWER 38 OF 126 MEDLINE
AN 94156180 MEDLINE
DN 94156180
TI Codon usage in Kluyveromyces lactis and in yeast cytochrome c-encoding genes.
AU Freire-Picos M A; Gonzalez-Siso M I; Rodriguez-Belmonte E; Rodriguez-Torres A M; Ramil E; Cerdan M E
CS Departamento de Biologia Celular y Molecular, Universidad de La Coruna, Spain..
SO GENE, **(1994 Feb 11)** 139 (1) 43-9.
Journal code: FOP. ISSN: 0378-1119.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199406
AB Codon usage (CU) in Kluyveromyces lactis has been studied. Comparison of CU in highly and lowly expressed genes reveals the existence of 21 **optimal** codons; 18 of them are also **optimal** in other yeasts like Saccharomyces cerevisiae or Candida albicans. Codon bias index (CBI) values have been recalculated with reference to the assignment of **optimal** codons in K. lactis and compared to those previously reported in the literature taking as reference the **optimal** codons from S. cerevisiae. A new index, the intrinsic codon deviation index (ICDI), is proposed to estimate codon bias of genes from species in which **optimal** codons are not known; its correlation with other index values, like CBI or effective number of codons (Nc), is high. A comparative analysis of CU in six cytochrome-c-encoding genes (CYC) from five yeasts is also presented and the differences found in the codon bias of these genes are discussed in relation to the metabolic type to which the corresponding yeasts belong. Codon bias in the CYC from K. lactis and S. cerevisiae is correlated to **mRNA** levels.
CT Check Tags: Comparative Study; Support, Non-U.S. Gov't
Amino Acids: ME, metabolism
Base Sequence
*Candida albicans: GE, genetics
Candida albicans: ME, metabolism
***Codon: ME, metabolism**
*Genes, Fungal
*Kluyveromyces: GE, genetics
Kluyveromyces: ME, metabolism

**RNA, Messenger: AN, analysis**
**RNA, Messenger: ME, metabolism**
*Saccharomyces cerevisiae: GE, genetics
Saccharomyces cerevisiae: ME, metabolism
Species Specificity
CN 0 (Amino Acids); 0 (Codon); 0 (**RNA**, Messenger)
GEN CYC; ACT; ADH1; ADH2; ADH3; ADH4; GAL7; GAL10; HHT1; IPP; KlCYC1; KLERD2; KlGAL11; KlGAP1; KlL25; KlKEX1; KlRP59; LAC4; LAC9; LEU2; RAG1; RAG2; SEC14; TRP1; URA3

L134 ANSWER 39 OF 126 MEDLINE
AN 94152169 MEDLINE
DN 94152169
TI Synonymous codon usage in Kluyveromyces lactis.
AU Lloyd A T; Sharp P M
CS Department of Genetics, Trinity College, Dublin, Ireland..
SO YEAST, **(1993 Nov)** 9 (11) 1219-28.
Journal code: YEA. ISSN: 0749-503X.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199405
AB The nature and variation of synonymous codon usage in 47 open reading frames from Kluyveromyces lactis have been investigated. Using multivariate statistical analysis, a single major trend among K. lactis genes was identified that differentiates among genes by expression level: highly expressed genes have high codon usage bias, while genes of low expression level have low bias. A relatively minor secondary trend differentiates among genes according to G+C content at silent sites. In these respects, K. lactis is similar to both Saccharomyces cerevisiae and Candida albicans, and the same **'optimal'** codons appear to be selected in highly expressed genes in all three species. In addition, silent sites in K. lactis and S. cerevisiae have similar G+C contents, but in C. albicans genes they are more A+T-rich. Thus, in all essential features, codon usage in K. lactis is very similar to that in S. cerevisiae, even though silent sites in genes compared between these two species have undergone sufficient mutation to be saturated with changes. We conclude that the factors influencing overall codon usage, namely mutational biases and the abundances of particular tRNAs, have not diverged between the two species. Nevertheless, in a few cases, codon usage differs between homologous genes from K. lactis and S. cerevisiae. The strength of codon usage bias in cytochrome c genes differs considerably, presumably because of different expression patterns in the two species. Two other, linked, genes have very different G+C content at silent sites in the two species, which may be a reflection of their chromosomal locations. Correspondence analysis was used to identify two open reading frames with highly atypical codon usage that are probably not genes.
CT Check Tags: Comparative Study; Support, Non-U.S. Gov't
Base Sequence
Candida albicans: GE, genetics
***Codon: GE, genetics**
Evolution
Genes, Fungal
*Kluyveromyces: GE, genetics
Open Reading Frames
**RNA, Fungal: GE, genetics**
Saccharomyces cerevisiae: GE, genetics
Species Specificity
CN 0 (Codon); 0 (**RNA**, Fungal)

L134 ANSWER 40 OF 126 MEDLINE
AN 94088561 MEDLINE
DN 94088561
TI Effect of sequence context at stop codons on efficiency of reinitiation in

GCN4 translational control.
AU Grant C M; Hinnebusch A G
CS Section on Molecular Genetics of Lower Eukaryotes, National Institute of Child Health and Human Development, Bethesda, Maryland 20892..
SO MOLECULAR AND CELLULAR BIOLOGY, **(1994 Jan)** 14 (1) 606-18.
Journal code: NGY. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199403
AB Translational control of the GCN4 gene involves two short open reading frames in the **mRNA** leader (uORF1 and uORF4) that differ greatly in the ability to allow reinitiation at GCN4 following their own translation. The low efficiency of reinitiation characteristic of uORF4 can be reconstituted in a hybrid element in which the last codon of uORF1 and 10 nucleotides 3' to its stop codon (the termination region) are substituted with the corresponding nucleotides from uORF4. To define the features of these 13 nucleotides that determine their effects on reinitiation, we separately randomized the sequence of the third codon and termination region of the uORF1-uORF4 hybrid and selected mutant alleles with the high-level reinitiation that is characteristic of uORF1. The results indicate that many different A+U-rich triplets present at the third codon of uORF1 can overcome the inhibitory effect of the termination region derived from uORF4 on the efficiency of reinitiation at GCN4. Efficient reinitiation is not associated with codons specifying a particular amino acid or isoacceptor tRNA. Similarly, we found that a diverse collection of A+U-rich sequences present in the termination region of uORF1 could restore efficient reinitiation at GCN4 in the presence of the third codon derived from uORF4. To explain these results, we propose that reinitiation can be impaired by **stable** base pairing between nucleotides flanking the uORF1 stop codon and either the tRNA which pairs with the third codon, the rRNA, or sequences located elsewhere in GCN4 **mRNA**. We suggest that these interactions delay the resumption of scanning following peptide chain termination at the uORF and thereby lead to ribosome dissociation from the **mRNA**.
CT Base Sequence
***Codon: GE, genetics**
Gene Expression Regulation, Fungal
*Genes, Fungal
Molecular Sequence Data
Mutagenesis, Insertional
Open Reading Frames
Peptide Chain Termination: GE, genetics
***RNA, Fungal: GE, genetics**
**RNA, Messenger: GE, genetics**
*Saccharomyces cerevisiae: GE, genetics
*Translation, Genetic
CN 0 (Codon); 0 (**RNA**, Fungal); 0 (**RNA**, Messenger)
GEN GCN4

L134 ANSWER 41 OF 126 MEDLINE
AN 94051567 MEDLINE
DN 94051567
TI Reduced synonymous substitution rate at the start of enterobacterial genes.
AU Eyre-Walker A; Bulmer M
CS Department of Biological Sciences, Rutgers University, Piscataway, NJ 08855-1059..
SO NUCLEIC ACIDS RESEARCH, **(1993 Sep 25)** 21 (19) 4599-603.
Journal code: O8L. ISSN: 0305-1048.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199402

AB Synonymous codon usage is less biased at the start of Escherichia coli genes than elsewhere. The rate of synonymous substitution between E.coli and Salmonella typhimurium is substantially reduced near the start of the gene, which suggests the presence of an additional selection pressure which competes with the selection for codons which are most rapidly translated. Possible competing sources of selection are the presence of secondary ribosome binding sites downstream from the start codon, the avoidance of **mRNA** secondary structure near the start of the gene and the use of sub-**optimal** codons to regulate gene expression. We provide evidence against the last of these possibilities. We also show that there is a decrease in the frequency of A, and an increase in the frequency of G along the E.coli genes at all three codon positions. We argue that these results are most consistent with selection to avoid **mRNA** secondary structure.

CT Check Tags: Comparative Study
Base Composition
***Codon**
DNA, Bacterial: GE, genetics
*Escherichia coli: GE, genetics
*Genes, Structural, Bacterial
*Salmonella typhimurium: GE, genetics
Selection (Genetics)

CN 0 (Codon); 0 (DNA, Bacterial)

L134 ANSWER 42 OF 126 MEDLINE
AN 93389723 MEDLINE
DN 93389723
TI The 3' codon context effect on UAG suppressor tRNA is different in Escherichia coli and human cells.
AU Phillips-Jones M K; Watson F J; Martin R
CS Krebs Institute for Biomolecular Research, University of Sheffield, Western Bank, U.K..
SO JOURNAL OF MOLECULAR BIOLOGY, **(1993 Sep 5)** 233 (1) 1-6.
Journal code: J6V. ISSN: 0022-2836.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199312

AB We have compared the effect of 3' context on the efficiency of nonsense suppressor tRNAs in Escherichia coli and human cells. Plasmids containing amber (UAG) termination codons were constructed in the vector pRSV beta gal by oligonucleotide insertion at an N-terminal location in a lacZ fusion. A family of identical vectors was prepared with either A, C, G or U as the first 3' base following the stop codon. These derivatives of pRSV beta gal were expressed in E. coli as **stable** plasmids, or transiently in human 293 cell tissue culture. Nonsense suppression was monitored using enzyme assays for beta-galactosidase. In E. coli the efficiency of a plasmid-borne bacterial tRNA(trp) UAG suppressor varied A > G > C = U. When the same lacZ reporter vectors were cotransfected with a human tRNA(ser) UAG suppressor plasmid into human cells, context effects of a different nature were detected. Double reciprocal analysis of dose-response experiments were used to show that the efficiency of suppression varied C > G > U = A. The discovery of different codon context effects on nonsense suppression in human cells suggest that the interaction between mammalian tRNAs or release factors and their target codons may have different characteristics from those in bacteria.

CT Check Tags: Comparative Study; Human; Support, Non-U.S. Gov't
beta-Galactosidase: BI, biosynthesis
beta-Galactosidase: GE, genetics
Base Sequence
Cells, Cultured
***Codon: GE, genetics**
*Escherichia coli: GE, genetics
Gene Expression Regulation
Genetic Vectors: GE, genetics

Molecular Sequence Data
Recombinant Fusion Proteins: BI, biosynthesis
***RNA, Transfer, Trp: GE, genetics**
*Suppression, Genetic
*Terminator Regions (Genetics): GE, genetics
Transfection
Translation, Genetic
CN EC 3.2.1.23 (beta-Galactosidase); 0 (Codon); 0 (Recombinant Fusion Proteins); 0 (**RNA**, Transfer, Trp)

L134 ANSWER 43 OF 126 MEDLINE
AN 93373326 MEDLINE
DN 93373326
TI A codon 248 p53 mutation retains tumor suppressor function as shown by enhancement of tumor growth by antisense p53.
AU Mukhopadhyay T; Roth J A
CS Department of Thoracic and Cardiovascular Surgery, University of Texas M. D. Anderson Cancer Center, Houston 77030.
NC RO1-CA45187 (NCI)
SO CANCER RESEARCH, **(1993 Sep 15)** 53 (18) 4362-6.
Journal code: CNF. ISSN: 0008-5472.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199312
AB Codon 248 in domain iv of the highly conserved region of the p53 gene is a frequent site of mutations associated with sporadic cancers and the familial cancer syndrome (Li-Fraumeni syndrome). Therefore, a characterization of the functional significance of a codon 248 mutation is of interest. We used antisense **RNA** methodology to study the role of the wild-type and mutated p53 gene in cell growth and tumorigenesis. We introduced wild-type p53 complementary DNA in sense or antisense orientation under control of a beta-actin promoter into human non-small cell lung cancer cell line H322a which has a codon 248 mutation (G to T) and WTH226b which has wild type p53. The biological properties and p53 expression of **stable** G418-resistant clones were analyzed. We observed that in both cell lines antisense **RNA** expression significantly reduced p53 **mRNA** and protein production; it also caused increases in growth rate in cell cultures and in tumorigenicity in nu/nu mice for both cell types, suggesting that the mechanism by which p53 suppresses cell proliferation and tumorigenesis is not always abrogated by a codon 248 mutation.
CT Check Tags: Animal; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Base Sequence
Cell Division
***Codon**
*Genes, p53
Mice
Molecular Sequence Data
*Mutation
*Neoplasms, Experimental: PA, pathology
***RNA, Antisense: PD, pharmacology**
Tumor Cells, Cultured
CN 0 (Codon); 0 (**RNA**, Antisense)
GEN p53

L134 ANSWER 44 OF 126 MEDLINE
AN 93344516 MEDLINE
DN 93344516
TI Transfer **RNA**-mediated suppression of stop codons in protoplasts and transgenic plants.
AU Carneiro V T; Pelletier G; Small I
CS Laboratoire de Biologie Cellulaire, INRA, Versailles, France..
SO PLANT MOLECULAR BIOLOGY, **(1993 Jul)** 22 (4) 681-90.

Journal code: A6O. ISSN: 0167-4412.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199311
AB We have developed a simple, rapid and sensitive assay for tRNA gene expression in plant cells. A plant tRNA(Leu) gene was site-specifically mutated to encode each of the three anticodon sequences (CUA, UUA and UCA) that recognize, respectively, the amber, ochre and opal stop codons. The suppression activity of these genes was detected by their ability to restore transient beta-glucuronidase (GUS) expression in tobacco protoplasts electroporated with GUS genes containing premature stop codons. Protoplasts co-electroporated with the amber suppressor tRNA gene and a GUS gene containing a premature amber stop codon showed up to 20-25% of the activity found in protoplasts transfected with the functional control GUS gene. Ochre and opal suppressors presented maximum efficiencies of less than 1%. This system could be adapted to examine transcription, processing or aminoacylation of tRNAs in plant cells. In addition, phenotypically normal, fertile tobacco plants expressing a **stably** incorporated amber suppressor tRNA gene have been obtained. This suppressor tRNA can be used to transactivate a target gene containing a premature amber stop codon by a factor of at least several hundred-fold.
CT Check Tags: Support, Non-U.S. Gov't
Amino Acid Sequence
**Anticodon: GE, genetics**
Base Sequence
***Codon: GE, genetics**
Glucuronidase: GE, genetics
Kanamycin Resistance: GE, genetics
Legumes: GE, genetics
Molecular Sequence Data
Mutation
*Peptide Chain Termination: GE, genetics
*Plants, Transgenic: GE, genetics
Protoplasts
**RNA, Transfer, Leu: BI, biosynthesis**
***RNA, Transfer, Leu: GE, genetics**
*Suppression, Genetic
Tobacco: GE, genetics
Transformation, Genetic
CN EC 3.2.1.31 (Glucuronidase); 0 (Anticodon); 0 (Codon); 0 (**RNA**, Transfer, Leu)

L134 ANSWER 45 OF 126 MEDLINE
AN 93287139 MEDLINE
DN 93287139
TI Neutral adaptation of the genetic code to double-strand coding.
AU Konecny J; Eckert M; Schoniger M; Hofacker G L
CS Tech University Munich, Garching, Federal Republic of Germany..
SO JOURNAL OF MOLECULAR EVOLUTION, **(1993 May)** 36 (5) 407-16.
Journal code: J76. ISSN: 0022-2844.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199309
AB We lay new foundations to the hypothesis that the genetic code is adapted to evolutionary retention of information in the antisense strands of natural DNA/**RNA** sequences. In particular, we show that the genetic code exhibits, beyond the neutral replacement patterns of amino acid substitutions, **optimal** properties by favoring simultaneous evolution of proteins encoded in DNA/**RNA** sense-antisense strands. This is borne out in the sense-antisense transformations of the codons of every amino acid which target amino acids physicochemically similar to each other. Moreover, silent mutations in the sense strand

generate conservative ones in its antisense counterpart and vice versa. Coevolution of proteins coded by complementary strands is shown to be a definite possibility, a result which does not depend on any physical interaction between the coevolving proteins. Likewise, the degree to which the present genetic code is dedicated to evolutionary sense-antisense tolerance is demonstrated by comparison with many randomized codes. Double-strand coding is quantified from an information-theoretical point of view.

CT Check Tags: Animal; Support, Non-U.S. Gov't
Adaptation, Biological
***Codon: GE, genetics**
DNA: GE, genetics
DNA, Antisense: GE, genetics
*Genetic Code: GE, genetics
Models, Genetic
Mutagenesis: GE, genetics

RN 9007-49-2 (DNA)
CN 0 (Codon); 0 (DNA, Antisense)

L134 ANSWER 46 OF 126 MEDLINE
AN 93274877 MEDLINE
DN 93274877
TI Accuracy of tRNA charging and codon: anticodon recognition; relative importance for cellular **stability**.
AU Kowald A; Kirkwood T B
CS Laboratory of Mathematical Biology, National Institute for Medical Research, Mill Hill, London, U.K.
SO JOURNAL OF THEORETICAL BIOLOGY, **(1993 Feb 21)** 160 (4) 493-508. Journal code: K8N. ISSN: 0022-5193.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199309
AB Cellular homeostasis and the mechanisms which control homeostasis are important for understanding such fundamental processes as ageing and the origin of life. Several models have studied the importance of accurate protein synthesis for cellular **stability**, but these models have not considered the complexities of the translation process in any detail. Here we develop a new model which describes the interplay between aminoacyl-tRNA (aatRNA) synthetases, the cellular pool of charged tRNAs and the process of codon: anticodon recognition. We also take the processive character of the ribosomes into account. In common with previous work, our model predicts that the cellular translation apparatus can either be **stable** or deteriorate progressively with time. However, because our model explicitly describes different subreactions of the overall translation process, we are also able to assess the relative importance of accurate tRNA charging and codon: anticodon recognition for cellular **stability**. It appears that the tRNA charging by the aatRNA synthetases plays the key role in controlling the long-term **stability** of the cell. Ribosomal errors are less important because error-prone ribosomes, being processive, produce mainly inactive proteins which do not contribute to error propagation within the translation machinery.

CT Check Tags: Animal
Amino Acyl-tRNA Ligases: ME, metabolism
***Anticodon: GE, genetics**
*Cell Physiology
*Cells: PH, physiology
***Codon: GE, genetics**
*Models, Genetic
Proteins: BI, biosynthesis
Ribosomes: ME, metabolism
***RNA, Transfer: GE, genetics**
Translation, Genetic: GE, genetics

RN **9014-25-9 (RNA, Transfer)**

CN EC 6.1.1. (Amino Acyl-tRNA Ligases); 0 (Anticodon); 0 (Codon); 0 (Proteins)

L134 ANSWER 47 OF 126 MEDLINE
AN 93204490 MEDLINE
DN 93204490
TI Synonymous codon preferences in bacteriophage T4: a distinctive use of transfer **RNAs** from T4 and from its host Escherichia coli.
AU Kunisawa T
CS Department of Applied Biological Sciences, Science University of Tokyo, Noda, Japan..
SO JOURNAL OF THEORETICAL BIOLOGY, **(1992 Dec 7)** 159 (3) 287-98.
Journal code: K8N. ISSN: 0022-5193.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199306
AB Codon usage data of bacteriophage T4 genes were compiled and synonymous codon preferences were investigated in comparison with tRNA availabilities in an infected cell. Since the genome of T4 is highly AT rich and its codon usage pattern is significantly different from that of its host Escherichia coli, certain codons of T4 genes need to be translated by appropriate host transfer **RNAs** present in minor amounts. To avoid this predicament, T4 phage seems to direct the synthesis of its own tRNA molecules and these phage tRNAs are suggested to supplement the host tRNA population with isoacceptors that are normally present in minor amounts. A positive correlation was found in that the frequency of E. coli **optimal** codons in T4 genes increases as the number of protein monomers per phage particle increases. A negative correlation was also found between the number of protein monomers per phage and the frequency of "T4 **optimal** codons", which are defined as those codons that are efficiently recognized by T4 tRNAs. From these observations it was proposed that tRNAs from the host are predominantly used for translation of highly expressed T4 genes while tRNAs from T4 tend to be used for translation of weakly expressed T4 genes. This distinctive tRNA-usage in T4 may be an **optimization** of translational efficiency, and an adjustment of T4-encoded tRNAs to the synonymous codon preferences, which are largely influenced by the high genomic AT-content, would have occurred during evolution.
CT *Bacteriophage T4: GE, genetics
***Codon: PH, physiology**
*Escherichia coli: GE, genetics
***RNA, Transfer: PH, physiology**
RN **9014-25-9 (RNA, Transfer)**
CN 0 (Codon)

L134 ANSWER 48 OF 126 MEDLINE
AN 93050236 MEDLINE
DN 93050236
TI Codon-anticodon pairing. A model for interacting codon-anticodon duplexes located at the ribosomal A- and P-sites.
AU Lim V I; Venclovas C
CS Institute of Protein Research, Russian Academy of Sciences, Pushchino, Moscow Region..
SO FEBS LETTERS, **(1992 Nov 23)** 313 (2) 133-7.
Journal code: EUH. ISSN: 0014-5793.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199302
AB The interaction between two codon-anticodon duplexes of the ribosomal A- and P-site-bound tRNAs is the key feature of the proposed model. This interaction prohibits non-canonical base pairing at the first and second positions of the codon and controls base pairing at the third position

(wobbling rules ensuing from the model are in good accord with those generated from experiments). The model is capable of predicting codon context effects. It follows from the model that modifications of the first anticodon residue of the P-site tRNA can affect the **stability** of the A-site duplex, and that the translation of a DNA single chain analogue of **mRNA** should be accompanied by non-canonical base pairing at all three positions of the codon. These predictions of the model can be subjected to experimental tests.

CT ***Anticodon**
*Base Composition
***Codon**
*Models, Structural
Nucleic Acid Conformation
Ribosomes

CN 0 (Anticodon); 0 (Codon)

L134 ANSWER 49 OF 126 MEDLINE
AN 92373749 MEDLINE
DN 92373749
TI Translation inhibition by an **mRNA** coding region secondary structure is determined by its proximity to the AUG initiation codon.
AU Liebhaber S A; Cash F; Eshleman S S
CS Howard Hughes Medical Institute, Department of Genetics, University of Pennsylvania, School of Medicine, Philadelphia 19104-6145..
SO JOURNAL OF MOLECULAR BIOLOGY, **(1992 Aug 5)** 226 (3) 609-21.
Journal code: J6V. ISSN: 0022-2836.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199211
AB In the present study we investigate the impact of highly **stable** coding region secondary structures on **mRNA** translation efficiency. By introducing antisense segments into the 3'non-translated region of human alpha-globin **mRNA** we are able to synthesize a series of transcripts in which site-specific secondary structures are introduced without altering the primary structure of the 5' non-translated region, the coding region, or the encoded protein product. Coding region duplexes in close proximity to the AUG initiation codon are found to inhibit translation severely to a degree equal to that of a duplex that extends into the 5' non-translated region. In contrast, **mRNAs** containing duplexes positioned further 3' in the coding region translate at levels that are significantly higher although are still below those of native alpha-globin **mRNA**. The primary determinant of translation inhibition by coding region duplexes appears to be the proximity of the duplex to the AUG initiation codon and reflects a parallel inhibition of monosome formation. These data demonstrate that extensive coding region secondary structures suppress translation to a minimal or to a substantial degree depending on their distance from the initiation codon.

CT Check Tags: Human
Base Sequence
Chromosome Deletion
***Codon: GE, genetics**
DNA: GE, genetics
*Globin: GE, genetics
Molecular Sequence Data
Mutagenesis, Site-Directed
Nucleic Acid Conformation
Nucleic Acid Heteroduplexes: CH, chemistry
Nucleic Acid Heteroduplexes: GE, genetics
Oligodeoxyribonucleotides
*Oligonucleotides, Antisense
Restriction Mapping
Ribonucleases
**RNA, Messenger: BI, biosynthesis**
**RNA, Messenger: CH, chemistry**

***RNA, Messenger: GE, genetics**
Suppression, Genetic
Transcription, Genetic
*Translation, Genetic: GE, genetics
RN 9004-22-2 (Globin); 9007-49-2 (DNA)
CN EC 3.1.- (Ribonucleases); 0 (Codon); 0 (Nucleic Acid Heteroduplexes); 0 (Oligodeoxyribonucleotides); 0 (Oligonucleotides, Antisense); 0 ( **RNA**, Messenger)

L134 ANSWER 50 OF 126 MEDLINE
AN 92249095 MEDLINE
DN 92249095
TI The relationship between metastatic phenotype and steady expression of BGC-Ha-ras oncogene from metastasis cell lines in nude mice (abstract).
AU Li Y J
CS Beijing Institute for Cancer Research.
SO CHUNG-HUA CHUNG LIU TSA CHIH [CHINESE JOURNAL OF ONCOLOGY], **(1992 Nov)** 13 (6) 402-5.
Journal code: EBH. ISSN: 0253-3766.
CY China
DT Journal; Article; (JOURNAL ARTICLE)
LA Chinese
FS Priority Journals
EM 199208
AB NIH/3T3 cells transformed by activated BGC-Ha-ras (6.6 kb) with a point mutation at codon 12 were able to induce tumor in nude mice with lung metastasis. The metastatic phenotype seemed **stable** in vivo metastasis assay. After two round subculture of the successively induced metastasis foci, two cell lines, GCM-1/3T3 and GCM-2/3T3, were established. In Southern blot analysis it was found that the bands from GCM-1/3T3 and GCM-2/3T3 were the same. Based on Southern analysis and polymerase chain reaction-restriction fragment length polymorphism (PCR-RPLF), it was proved that the activated c-Ha-ras (6.6 kb) existed all along in the genomes of the transformed and metastatic culture cells. Amplification and over-expression of activated c-Ha-ras were shown by DNA and **RNA** dot blot hybridization in transformed and metastatic culture cells. The metastatic phenotype might be related to the existence and steady expression of the point mutated ras.
CT Check Tags: Animal; Human
*Cell Transformation, Neoplastic: GE, genetics
***Codon: GE, genetics**
English Abstract
Fibrosarcoma: PA, pathology
Gene Expression Regulation, Neoplastic
*Genes, ras: PH, physiology
Mice
Mice, Inbred Strains
Mice, Nude
*Neoplasm Metastasis: GE, genetics
Polymerase Chain Reaction
Polymorphism, Restriction Fragment Length
Proto-Oncogene Protein p21(ras): GE, genetics
Stomach Neoplasms: PA, pathology
Tumor Cells, Cultured
CN EC 3.6.1.- (Proto-Oncogene Protein p21(ras)); 0 (Codon)

L134 ANSWER 51 OF 126 MEDLINE
AN 92224276 MEDLINE
DN 92224276
TI Codon usage is imposed by the gene location in the transcription unit.
AU Delorme M O; Henaut A
CS Centre de Genetique Moleculaire, Laboratoire propre du CNRS associe `a l'Universite Pierre et Marie Curie, Paris VI, Gif-sur-Yvette, France..
SO CURRENT GENETICS, **(1991 Nov)** 20 (5) 353-8.
Journal code: CUG. ISSN: 0172-8083.
CY United States

DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199207
AB A characteristic profile of the fluctuations of codon usage is observed in bacteriophages and mitochondria. By following the DNA in the direction of transcription, one moves slowly from a region where selective pressure favours codons ending with C to a region where the bias is in favour of codons ending with T; then, abruptly, one again enters a region of codons ending in C. The transcription end point takes place in the area of abrupt change in codon usage. By comparing Drosophila yakuba and mouse mitochondrial genomes, it is possible to show that the strategy of codon usage for a given gene depends on its location along the transcription unit and not on the encoded protein. The choice of codons ending in T or C allows large scale variations of DNA **stability** which could regulate the speed of propagation of the **RNA** polymerase.
CT Check Tags: Animal; Comparative Study; Human
Bacteriophages: GE, genetics
Chromosome Mapping
***Codon**
Drosophila: GE, genetics
DNA, Mitochondrial
Mice
*Mitochondria: ME, metabolism
Selection (Genetics)
*Transcription, Genetic
CN 0 (Codon); 0 (DNA, Mitochondrial)

L134 ANSWER 52 OF 126 MEDLINE
AN 92175524 MEDLINE
DN 92175524
TI Efficient synthesis of secreted murine interleukin-2 by Saccharomyces cerevisiae: influence of 3'-untranslated regions and codon usage.
AU Demolder J; Fiers W; Contreras R
CS Laboratory of Molecular Biology, State University, Gent, Belgium..
SO GENE, **(1992 Feb 15)** 111 (2) 207-13.
Journal code: FOP. ISSN: 0378-1119.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199206
AB Several expression vectors were compared which directed the synthesis of secreted murine interleukin-2 (mIL2) in the culture medium of Saccharomyces cerevisiae. We used the prepro-sequence of the alpha 1 mating-factor precursor as a secretion signal in S. cerevisiae in combination with different promoters. The yield of mature mIL2 was significantly improved by deleting the major part of the 3'-untranslated region (UTR). In Northern-blotting experiments we showed that a destabilizing sequence present in the 3' UTR might be responsible for rapid degradation of the mIL2 **mRNA**. The highest expression (about 10 micrograms/ml) was obtained under control of the GAL1 promoter in an S. cerevisiae strain where the regulatory GAL4 gene was overexpressed. No difference in expression level was observed in a construct wherein twelve consecutive codons were replaced by **optimal** codons for S. cerevisiae.
CT Check Tags: Animal; Support, Non-U.S. Gov't
Base Sequence
Blotting, Northern
***Codon: GE, genetics**
Fungal Proteins: GE, genetics
*Gene Expression Regulation, Fungal: GE, genetics
*Genetic Vectors: GE, genetics
Interleukin-2: BI, biosynthesis
*Interleukin-2: GE, genetics
Interleukin-2: SE, secretion

Mice
Molecular Sequence Data
Peptides: GE, genetics
Plasmids: GE, genetics
Promoter Regions (Genetics): GE, genetics
Protein Precursors: GE, genetics
*Saccharomyces cerevisiae: GE, genetics
Transcription Factors: GE, genetics
RN 61194-02-3 (mating factor)
CN 0 (Codon); 0 (Fungal Proteins); 0 (GAL4 protein, Saccharomyces); 0 (Interleukin-2); 0 (Peptides); 0 (Plasmids); 0 (Protein Precursors); 0 (Transcription Factors)
GEN mIL2; GAL1; GAL4

L134 ANSWER 53 OF 126 MEDLINE
AN 92102673 MEDLINE
DN 92102673
TI Evaluation of foreign gene codon **optimization** in yeast: expression of a mouse IG kappa chain.
AU Kotula L; Curtis P J
CS Wistar Institute of Anatomy and Biology, Philadelphia, PA 19104..
SO BIO/TECHNOLOGY, **(1991 Dec)** 9 (12) 1386-9.
Journal code: AL1. ISSN: 0733-222X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS B
EM 199204
AB We have **optimized** the codons in an immunoglobulin kappa chain gene to those preferred in the yeast Saccharomyces cerevisiae. The mutant and wild type kappa chain genes were each fused with a synthetic invertase signal peptide that also contained only yeast-preferred codons, and expressed in the F762 yeast strain. The use of yeast-preferred codons resulted in a more than 5-fold increase in the rate of synthesis and at least a 50-fold increase in the steady state level of protein.
CT Check Tags: Animal; Comparative Study; Support, Non-U.S. Gov't
Biotechnology
***Codon: GE, genetics**
DNA: GE, genetics
Gene Expression
Immunoglobulins, kappa-Chain: BI, biosynthesis
*Immunoglobulins, kappa-Chain: GE, genetics
Mice
**RNA, Fungal: GE, genetics**
**RNA, Fungal: ME, metabolism**
**RNA, Messenger: ME, metabolism**
*Saccharomyces cerevisiae: GE, genetics
Signal Peptides: GE, genetics
RN 9007-49-2 (DNA)
CN 0 (Codon); 0 (Immunoglobulins, kappa-Chain); 0 (**RNA**, Fungal); 0 (**RNA**, Messenger); 0 (Signal Peptides)

L134 ANSWER 54 OF 126 MEDLINE
AN 92084103 MEDLINE
DN 92084103
TI The product of the yeast UPF1 gene is required for rapid turnover of **mRNAs** containing a premature translational termination codon.
AU Leeds P; Peltz S W; Jacobson A; Culbertson M R
CS Laboratories of Genetics and Molecular Biology, University of Wisconsin, Madison 53706..
NC GM26217 (NIGMS)
GM27757 (NIGMS)
GM07133 (NIGMS)
SO GENES AND DEVELOPMENT, **(1991 Dec)** 5 (12A) 2303-14.
Journal code: FN3. ISSN: 0890-9369.
CY United States

DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199203
AB **mRNA** decay rates often increase when translation is terminated prematurely due to a frameshift or nonsense mutation. We have identified a yeast gene, UPF1, that codes for a trans-acting factor whose function is necessary for enhanced turnover of **mRNAs** containing a premature stop codon. In the absence of UPF1 function, frameshift or nonsense mutations in the HIS4 or LEU2 genes that normally cause rapid **mRNA** decay fail to have this effect. Instead, the **mRNAs** decay at rates similar to the corresponding wild-type **mRNAs**. The **stabilization** of frameshift or nonsense **mRNAs** observed in upf1- strains does not appear to result from enhanced readthrough of the termination signal. Loss of UPF1 function has no effect on the accumulation or **stability** of HIS4+ or LEU2+ **mRNA**, suggesting that the UPF1 product functions only in response to a premature termination signal. When we examined the accumulation and **stability** of other wild-type **mRNAs** in the presence or absence of UPF1, including MAT alpha 1, STE3, ACT1, PGK1, PAB1, and URA3 **mRNAs**, only the URA3 transcript was affected. On the basis of these and other results, the UPF1 product appears to participate in a previously uncharacterized pathway leading to the degradation of a limited class of yeast transcripts.
CT Check Tags: Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Base Sequence
Cloning, Molecular
***Codon**
DNA
Fungal Proteins: GE, genetics
Histidine: GE, genetics
Molecular Sequence Data
Mutation
*Peptide Chain Termination
Plasmids
Ribosomes: ME, metabolism
***RNA, Fungal: ME, metabolism**
***RNA, Messenger: ME, metabolism**
*Saccharomyces cerevisiae: GE, genetics
Terminator Regions (Genetics)
Translation, Genetic
RN 7006-35-1 (Histidine); 9007-49-2 (DNA)
CN 0 (Codon); 0 (Fungal Proteins); 0 (Plasmids); 0 (**RNA**, Fungal); 0 (**RNA**, Messenger)
GEN UPF1

L134 ANSWER 55 OF 126 MEDLINE
AN 92042179 MEDLINE
DN 92042179
TI Nitrate-inducible formate dehydrogenase in Escherichia coli K-12. II. Evidence that a **mRNA** stem-loop structure is essential for decoding opal (UGA) as selenocysteine.
AU Berg B L; Baron C; Stewart V
CS Section of Microbiology, Cornell University, Ithaca, New York 14853-8101.
NC GM36877 (NIGMS)
SO JOURNAL OF BIOLOGICAL CHEMISTRY, **(1991 Nov 25)** 266 (33) 22386-91.
Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199202
AB fdnG, encoding the selenopeptide of Escherichia coli formate dehydrogenase-N, contains an in-frame opal (UGA) codon at amino acid position 196 that directs selenocysteine incorporation. We have identified

sequences that contribute to the **mRNA** context required for decoding this UGA as selenocysteine. We identified a potential stem-loop structure immediately downstream of UGA196 that is comparable in size and structure to a stem-loop predicted to form in fdhF, which encodes the selenopeptide of E. coli formate dehydrogenase-H. Mutational analysis of the fdnG stem-loop structure suggests that it is critical for decoding UGA196 as selenocysteine. Our data indicate that both **stability** and specific nucleotide sequences of the stem-loop likely contribute to the appropriate **mRNA** context for selenocysteine incorporation into the fdnG gene product.

CT Check Tags: Comparative Study; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Base Composition
Base Sequence
Cloning, Molecular
***Codon: GE, genetics**
*Cysteine: AA, analogs & derivatives
Cysteine: ME, metabolism
Enzyme Induction
Escherichia coli: DE, drug effects
Escherichia coli: EN, enzymology
*Escherichia coli: GE, genetics
Formate Dehydrogenases: BI, biosynthesis
*Formate Dehydrogenases: GE, genetics
Genotype
Molecular Sequence Data
Mutagenesis, Site-Directed
*Nitrates: PD, pharmacology
Nucleic Acid Conformation
Oligodeoxyribonucleotides
*Organoselenium Compounds: ME, metabolism
Plasmids
***RNA, Messenger: GE, genetics**
**RNA, Messenger: ME, metabolism**

RN 10236-58-5 (Selenocysteine); 52-90-4 (Cysteine)

CN EC 1.2.1.2 (Formate Dehydrogenases); 0 (Codon); 0 (Nitrates); 0 (Oligodeoxyribonucleotides); 0 (Organoselenium Compounds); 0 (Plasmids); 0 (**RNA**, Messenger)

GEN fdhF; fdnG

L134 ANSWER 56 OF 126 MEDLINE

AN 91355866 MEDLINE

DN 91355866

TI Analysis of leaky viral translation termination codons in vivo by transient expression of improved beta-glucuronidase vectors.

AU Skuzeski J M; Nichols L M; Gesteland R F

CS Howard Hughes Medical Institute, University of Utah School of Medicine, Salt Lake City 84132..

SO PLANT MOLECULAR BIOLOGY, **(1990 Jul)** 15 (1) 65-79.
Journal code: A6O. ISSN: 0167-4412.

CY Netherlands

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199112

AB Plant **RNA** viruses commonly exploit leaky translation termination signals in order to express internal protein coding regions. As a first step to elucidate the mechanism(s) by which ribosomes bypass leaky stop codons in vivo, we have devised a system in which readthrough is coupled to the transient expression of beta-glucuronidase (GUS) in tobacco protoplasts. GUS vectors that contain the stop codons and surrounding nucleotides from the readthrough regions of several different **RNA** viruses were constructed and the plasmids were tested for the ability to direct transient GUS expression. These studies indicated that ribosomes bypass the leaky termination sites at efficiencies ranging from essentially 0 to ca. 5% depending upon the viral sequence. The results

suggest that the efficiency of readthrough is determined by the sequence surrounding the stop codon. We describe improved GUS expression vectors and **optimized** transfection conditions which made it possible to assay low-level translational events.

CT Base Sequence
***Codon: GE, genetics**
DNA, Viral: GE, genetics
Genetic Vectors
Glucuronidase: GE, genetics
Molecular Sequence Data
Peptide Chain Termination
Plant Viruses: EN, enzymology
*Plant Viruses: GE, genetics
Tobacco: EN, enzymology
Tobacco: GE, genetics
*Translation, Genetic
CN EC 3.2.1.31 (Glucuronidase); 0 (Codon); 0 (DNA, Viral)

L134 ANSWER 57 OF 126 MEDLINE
AN 91334248 MEDLINE
DN 91334248
TI Codon usage and secondary structure of **mRNA**.
AU Zama M
CS Division of Biology, National Institute of Radiological Sciences, Chiba-shi, Japan..
SO NUCLEIC ACIDS SYMPOSIUM SERIES, **(1990)** (22) 93-4.
Journal code: O8N. ISSN: 0261-3166.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199111
AB The specific codon usage pattern of the repetitive unit nucleotide sequence of silk fibroin **mRNA** suggests that selection has operated on the codon usage to **optimize** the secondary structure characteristic of the **mRNA**. The correlation between the **stability** map of local secondary structure of type I collagen **mRNA** and the codon usage pattern and the translation rate of the collagen is also implied.
CT Check Tags: Animal
***Codon**
Evolution
Fibroin: GE, genetics
Nucleic Acid Conformation
Nucleic Acid Denaturation
Repetitive Sequences, Nucleic Acid
**RNA, Messenger: CH, chemistry**
***RNA, Messenger: GE, genetics**
Silkworms: GE, genetics
Translation, Genetic
RN 9007-76-5 (Fibroin)
CN 0 (Codon); 0 (**RNA**, Messenger)

L134 ANSWER 58 OF 126 MEDLINE
AN 91334193 MEDLINE
DN 91334193
TI Assignments of the iminoproton resonances of Bombyx mori tRNA(UCCGly) and the comparison of its structure and **stability** with those of tRNA(GCCGly).
AU Amano M; Kyogoku Y; Kawakami M
CS Institute for Protein Research, Osaka University, Japan.
SO NUCLEIC ACIDS SYMPOSIUM SERIES, **(1990)** (22) 111-2.
Journal code: O8N. ISSN: 0261-3166.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English

FS Priority Journals
EM 199111
AB Most of the iminoproton resonances in the 1H-NMR spectrum of Bombyx mori tRNA(UCCGly) have been assigned by the sequential NOEs. Any peak which indicates the presence of the tertiary GC base pair between the D and T loops could not be detected. The effects of temperature and the addition of magnesium ions and spermine on the 1H-NMR spectrum of this tRNA were examined. From the temperature change, it was found that the acceptor stem and the D stem in Bombyx mori tRNA(UCCGly) are equally **stable** even in the absence of magnesium, which is different from tRNA(GCCGly) where the D stem is not so **stable**.
CT Check Tags: Animal
Base Sequence
***Codon**
Magnesium: PD, pharmacology
Molecular Sequence Data
Nuclear Magnetic Resonance
Nucleic Acid Conformation
***RNA, Transfer, Gly: CH, chemistry**
Silkworms
Spermine: PD, pharmacology
Thermodynamics
RN 71-44-3 (Spermine); 7439-95-4 (Magnesium)
CN 0 (Codon); 0 (**RNA**, Transfer, Gly)

L134 ANSWER 59 OF 126 MEDLINE
AN 91309730 MEDLINE
DN 91309730
TI Codon bias and gene expression.
AU Kurland C G
CS Department of Molecular Biology, Uppsala University, Sweden..
SO FEBS LETTERS, **(1991 Jul 22)** 285 (2) 165-9. Ref: 48
Journal code: EUH. ISSN: 0014-5793.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals; Cancer Journals
EM 199110
AB The frequencies with which individual synonymous codons are used to code their cognate amino acids is quite variable from genome to genome and within genomes, from gene to gene. One particularly well documented codon bias is that associated with highly expressed genes in bacteria as well as in yeast; this is the so-called major codon bias. Here, it is suggested that the major codon bias is not an arrangement for regulating individual gene expression. Instead, the data suggest that this codon bias, which is correlated with a corresponding bias of tRNA abundance, is a global arrangement for **optimizing** the growth efficiency of cells. On the practical side, it is suggested that heterologous gene expression is not as sensitive to codon bias as previously thought, but that it is quite sensitive to other characteristics of the heterologous gene.
CT Check Tags: Support, Non-U.S. Gov't
***Codon**
Escherichia coli: GE, genetics
*Gene Expression
Proteins: ME, metabolism
**RNA, Messenger: ME, metabolism**
**RNA, Transfer, Amino Acyl: ME, metabolism**
Saccharomyces cerevisiae: GE, genetics
*Translation, Genetic
CN 0 (Codon); 0 (**RNA**, Messenger); 0 (**RNA**, Transfer, Amino Acyl)

L134 ANSWER 60 OF 126 MEDLINE
AN 91289687 MEDLINE

DN 91289687
TI Influence of the codon following the initiation codon on the expression of the lacZ gene in Saccharomyces cerevisiae.
AU Looman A C; Laude M; Stahl U
CS Institut fur Garungsgewerbe und Biotechnologie, Berlin, FRG..
SO YEAST, **(1991 Feb)** 7 (2) 157-65.
Journal code: YEA. ISSN: 0749-503X.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199110
AB A set of 32 different codons were introduced in a lacZ expression vector (pPTK400) immediately 3' from the AUG initiation codon. Expression of the lacZ gene was determined in Saccharomyces cerevisiae by measuring the amount of beta-galactosidase fusion protein using immuno-gel electrophoresis. A 5.3-fold difference in expression was found among the various constructs. It was found that there was no preference for a certain nucleotide in any position of the second codon and there was no distinct correlation between the level of tRNA corresponding to any particular second codon and expression. No correlation could be found between the local secondary structure and expression. When the overall codon usage in yeast and the codon usage in the second position of the **mRNA** is compared, there is no obvious significant difference in preference. This indicates that in yeast, in contrast to Escherichia coli, the codon choice at the beginning of the **mRNA** does not deviate from the one further downstream and is determined by the requirements for **optimal** translation elongation. Important determinants of the **optimal** context for an initiation codon in yeast therefore must be located mainly 5' from this codon.
CT beta-Galactosidase: BI, biosynthesis
Amino Acid Sequence
Base Sequence
Binding Sites
***Codon: GE, genetics**
Consensus Sequence
Escherichia coli: GE, genetics
*Gene Expression Regulation, Fungal
Immunoelectrophoresis
*Lac Operon
Molecular Sequence Data
Nucleic Acid Conformation
Plasmids
Recombinant Fusion Proteins: BI, biosynthesis
Ribosomes: ME, metabolism
**RNA, Messenger: GE, genetics**
Saccharomyces cerevisiae: GE, genetics
Transformation, Genetic
*Translation, Genetic
CN EC 3.2.1.23 (beta-Galactosidase); 0 (Codon); 0 (Plasmids); 0 (Recombinant Fusion Proteins); 0 (**RNA**, Messenger)
GEN lacZ

L134 ANSWER 61 OF 126 MEDLINE
AN 91203897 MEDLINE
DN 91203897
TI Nonsense codons within the Rous sarcoma virus gag gene decrease the **stability** of unspliced viral **RNA**.
AU Barker G F; Beemon K
CS Department of Biology, Johns Hopkins University, Baltimore, Maryland 21218.
NC CA-48746 (NCI)
5T32GM07231 (NIGMS)
SO MOLECULAR AND CELLULAR BIOLOGY, **(1991 May)** 11 (5) 2760-8.
Journal code: NGY. ISSN: 0270-7306.
CY United States

DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199107
AB The intracellular accumulation of the unspliced **RNA** of Rous sarcoma virus was decreased when translation was prematurely terminated by the introduction of nonsense codons within its 5' proximal gene, the gag gene. In contrast, the levels of spliced viral **RNAs** were not affected in our transient expression assays in chicken cells. Experiments using the transcription inhibitor dactinomycin showed that mutant unspliced **RNAs** were degraded more rapidly than wild-type **RNA**. Furthermore, mutant **RNAs** could be partially **stabilized** by coexpression of wild-type gag proteins in trans; however, intact gag proteins were not required to maintain the **stability** of **RNAs** which did not contain premature termination codons. Thus, termination codons seemed to destabilize the **RNA** not because of their effect on gag protein function but instead because they disrupted the process of translating the gag region of the **RNA**. Analysis of double-mutant constructs containing both deletions and termination codons within the gag gene also suggested that the **stability** of the unspliced **RNA** was affected by a cis-acting interaction between the **RNA** and ribosomes.
CT Check Tags: Animal; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Cells, Cultured
Chick Embryo
Chromosome Deletion
Cloning, Molecular
***Codon: GE, genetics**
Fibroblasts
*Genes, gag
Mutagenesis, Insertional
Plasmids
Restriction Mapping
**RNA Splicing**
***RNA, Viral: GE, genetics**
**RNA, Viral: ME, metabolism**
*Sarcoma Viruses, Avian: GE, genetics
Transcription, Genetic
Transfection
Translation, Genetic
CN 0 (Codon); 0 (Plasmids); 0 (**RNA**, Viral)
GEN gag

L134 ANSWER 62 OF 126 MEDLINE
AN 91200668 MEDLINE
DN 91200668
TI Effects of second-codon mutations on expression of the insulin-like growth factor-II-encoding gene in Escherichia coli.
AU Cantrell A S; Burgett S G; Cook J A; Smith M C; Hsiung H M
CS Department of Molecular Biology, Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46285..
SO GENE, **(1991 Feb 15)** 98 (2) 217-23.
Journal code: FOP. ISSN: 0378-1119.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199107
AB Expression plasmids encoding random sequence mutant proteins of insulin-like growth factor II (IGFII) were constructed by cassette mutagenesis, to improve the efficiency of IGFII synthesis in Escherichia coli. A pool of oligodeoxyribonucleotide linkers containing random trinucleotide sequences were used to introduce second-codon substitutions into the gene encoding Met-Xaa-Trp-IGFII in expression vectors. E. coli RV308 cells transformed with these vectors synthesized IGFII at levels varying from 0-22% of total cell protein. This variable synthesis is a

function of the random second-codon sequence and its corresponding amino acid, Xaa. Our data showed that **mRNA stability**, protein **stability** and translational efficiency all contributed to variable expression levels of Met-Xaa-Trp-IGFII in E. coli. Furthermore, an efficiently synthesized IGFII mutant protein, Met-His-Trp-IGFII, was converted to natural sequence IGFII by a simple oxidative cleavage reaction.

CT Check Tags: Human
Amino Acid Sequence
Base Sequence
***Codon: GE, genetics**
*Escherichia coli: GE, genetics
Gene Expression
Genetic Vectors
Insulin-Like Growth Factor II: BI, biosynthesis
*Insulin-Like Growth Factor II: GE, genetics
Molecular Sequence Data
*Mutagenesis, Insertional
Protein Processing, Post-Translational
Recombinant Proteins: BI, biosynthesis
**RNA, Messenger: GE, genetics**
Transcription, Genetic
Translation, Genetic

RN 67763-97-7 (Insulin-Like Growth Factor II)
CN 0 (Codon); 0 (Recombinant Proteins); 0 (**RNA**, Messenger)

L134 ANSWER 63 OF 126 MEDLINE
AN 91002660 MEDLINE
DN 91002660
TI Frameshifting at the internal stop codon within the **mRNA** for bacterial release factor-2 on eukaryotic ribosomes.
AU Donly C; Williams J; Richardson C; Tate W
CS Department of Biochemistry, University of Otago, Dunedin, New Zealand.
SO BIOCHIMICA ET BIOPHYSICA ACTA, **(1990 Aug 27)** 1050 (1-3) 283-7.
Journal code: A0W. ISSN: 0006-3002.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199101
AB A translational frameshift is necessary in the synthesis of Escherichia coli release factor 2 (RF-2) to bypass an in-frame termination codon within the coding sequence. High-efficiency frameshifting around this codon can occur on eukaryotic ribosomes as well as prokaryotic ribosomes. This was determined from the relative efficiency of translation of RF-2 **RNA** compared with that for the other release factor RF-1, which lacks the in-frame premature stop codon. Since the termination product is unstable an absolute measure of the efficiency of frameshifting has not been possible. A gene fusion between trpE and RF-2 was carried out to give a **stable** termination product as well as the frameshift product, thereby allowing a direct determination of frameshifting efficiency. The extension of RF-2 **RNA** near its start codon with a fragment of the trpE gene, while still allowing high efficiency frameshifting on prokaryotic ribosomes, surprisingly gives a different estimate of frameshifting on the eukaryotic ribosomes than that obtained with RF-2 **RNA** alone. This paradox may be explained by long distance context effects on translation rates in the frameshift region created by the trpE sequences in the gene fusion, and may reflect that pausing and translation rate are fundamental factors in determining the efficiency of frameshifting.

CT Check Tags: Support, Non-U.S. Gov't
Base Sequence
Cloning, Molecular
***Codon**
Escherichia coli: GE, genetics
*Escherichia coli: ME, metabolism

*Frameshift Mutation
Kinetics
Molecular Sequence Data
Oligonucleotide Probes
Peptide Termination Factors: BI, biosynthesis
*Peptide Termination Factors: GE, genetics
Recombinant Fusion Proteins: BI, biosynthesis
*Ribosomes: ME, metabolism
***RNA, Messenger: GE, genetics**
*Translation, Genetic
CN 0 (peptide chain termination release factor 2); 0 (Codon); 0 (Oligonucleotide Probes); 0 (Peptide Termination Factors); 0 (Recombinant Fusion Proteins); 0 (**RNA**, Messenger)

L134 ANSWER 64 OF 126 MEDLINE
AN 90221871 MEDLINE
DN 90221871
TI Suppression of the negative effect of minor arginine codons on gene expression; preferential usage of minor codons within the first 25 codons of the Escherichia coli genes.
AU Chen G F; Inouye M
CS Department of Biochemistry, Robert Wood Johnson Medical School-UMDNJ, Rutgers, Piscataway 08854..
NC GM 19043 (NIGMS)
SO NUCLEIC ACIDS RESEARCH, **(1990 Mar 25)** 18 (6) 1465-73.
Journal code: O8L. ISSN: 0305-1048.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199007
AB AGA and AGG codons for arginine are the least used codons in Escherichia coli, which are encoded by a rare tRNA, the product of the dnaY gene. We examined the positions of arginine residues encoded by AGA/AGG codons in 678 E. coli proteins. It was found that AGA/AGG codons appear much more frequently within the first 25 codons. This tendency becomes more significant in those proteins containing only one AGA or AGG codon. Other minor codons such as CUA, UCA, AGU, ACA, GGA, CCC and AUA are also found to be preferentially used within the first 25 codons. The effects of the AGG codon on gene expression were examined by inserting one to five AGG codons after the 10th codon from the initiation codon of the lacZ gene. The production of beta-galactosidase decreased as more AGG codons were inserted. With five AGG codons, the production of beta-galactosidase (Gal-AGG5) completely ceased after a mid-log phase of cell growth. After 22 hr induction of the lacZ gene, the overall production of Gal-AGG5 was 11% of the control production (no insertion of arginine codons). When five CGU codons, the major arginine codon were inserted instead of AGG, the production of beta-galactosidase (Gal-CGU5) continued even after stationary phase and the overall production was 66% of the control. The negative effect of the AGG codons on the Gal-AGG5 production was found to be dependent upon the distance between the site of the AGG codons and the initiation codon. As the distance was increased by inserting extra sequences between the two codons, the production of Gal-AGG5 increased almost linearly up to 8 fold. From these results, we propose that the position of the minor codons in an **mRNA** plays an important role in the regulation of gene expression possibly by modulating the **stability** of the initiation complex for protein synthesis.
CT Check Tags: Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
*beta-Galactosidase: GE, genetics
Amino Acid Sequence
*Arginine
Base Sequence
***Codon: GE, genetics**
Escherichia coli: EN, enzymology
*Escherichia coli: GE, genetics
*Galactosidases: GE, genetics

*Gene Expression
*Genes, Bacterial
Molecular Sequence Data
Oligonucleotide Probes
Plasmids
Restriction Mapping
***RNA, Messenger: GE, genetics**
*Suppression, Genetic
RN 7004-12-8 (Arginine)
CN EC 3.2.1.- (Galactosidases); EC 3.2.1.23 (beta-Galactosidase); 0 (Codon); 0 (Oligonucleotide Probes); 0 (Plasmids); 0 (**RNA**, Messenger)

L134 ANSWER 65 OF 126 MEDLINE
AN 90211260 MEDLINE
DN 90211260
TI Codon usage pattern in alpha 2(I) chain domain of chicken type I collagen and its implications for the secondary structure of the **mRNA** and the synthesis pauses of the collagen.
AU Zama M
CS Biology Division, National Institute of Radiological Sciences, Chiba-shi, Japan..
SO BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, **(1990 Mar 16)** 167 (2) 772-6.
Journal code: 9Y8. ISSN: 0006-291X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199007
AB A **stability** map of local secondary structure of the **mRNA** of the triple-helical alpha 2(I) chain domain of chicken type I collagen was obtained by plotting the free energy of the **optimal** secondary structure of a local segment in **mRNA** against the segment position along a base sequence of the **mRNA**. It was found that the positions of the minima of free energy in the plot coincide with the positions where synthesis pauses of the alpha-chain polypeptides of the corresponding sizes translated from the **mRNA** have been reported to occur (1). The codon usage pattern of each of the three major amino acids of the alpha-chain domain of the collagen, Gly, Pro and Ala, fluctuates considerably along the base sequence segments of the **mRNA** and a deviation of the pattern from that of the average of the whole alpha 2(I) chain domain **mRNA**, particularly for Gly codons, leads to a loss of the **stability** of the local secondary structure of the **mRNA**. The results suggest that selection has operated on the codon usage to **optimize** the secondary structure characteristic of the **mRNA** of the chicken collagen alpha 2(I) chain domain which leads to a nonuniform polypeptide elongation pattern.
CT Check Tags: Animal
Chickens
***Codon: GE, genetics**
Collagen: BI, biosynthesis
*Collagen: GE, genetics
*Genes, Structural
Macromolecular Systems
*Nucleic Acid Conformation
*Procollagen: GE, genetics
***RNA, Messenger: GE, genetics**
RN 9007-34-5 (Collagen)
CN 0 (Codon); 0 (Macromolecular Systems); 0 (Procollagen); 0 (**RNA**, Messenger)

L134 ANSWER 66 OF 126 MEDLINE
AN 90189181 MEDLINE
DN 90189181
TI Doublet preference and gene evolution.
AU Hanai R; Wada A

CS Department of Physics, Faculty of Science, University of Tokyo, Japan..
SO JOURNAL OF MOLECULAR EVOLUTION, **(1990 Feb)** 30 (2) 109-15.
Journal code: J76. ISSN: 0022-2844.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199006
AB Doublet preference analysis was carried out on coding and noncoding regions of Escherichia coli, Saccharomyces cerevisiae, and human mitochondrial and nuclear DNA. The preference pattern in 1-2 and 2-3 doublets in E. coli and S. cerevisiae correlated with that in noncoding regions. The 3-1 doublet preference in E. coli genes with low **optimal** codon frequency and in S. cerevisiae genes also showed a correlation with each of their noncoding doublet preference. A mechanism to explain these double preference correlations in doublet preference is presented: mutational biases, the origin of the noncoding region doublet preference, evolved so as to maintain the 1-2 and 2-3 doublet preference, which is determined by codon usage. These biases then acted on the 3-1 doublet, which was almost free of coding constraints, resulting in a similar preference in this doublet.
CT Check Tags: Comparative Study; Human; Support, Non-U.S. Gov't
Base Composition
***Codon: GE, genetics**
DNA, Bacterial: GE, genetics
DNA, Fungal: GE, genetics
DNA, Mitochondrial: GE, genetics
Escherichia coli: GE, genetics
*Evolution
***RNA, Messenger: GE, genetics**
Saccharomyces cerevisiae: GE, genetics
Species Specificity
CN 0 (Codon); 0 (DNA, Bacterial); 0 (DNA, Fungal); 0 (DNA, Mitochondrial); 0 (**RNA**, Messenger)

L134 ANSWER 67 OF 126 MEDLINE
AN 90136256 MEDLINE
DN 90136256
TI Codon evolution and conservation of the reading phase in genetic code translation.
AU Toha J C; Donoso R; Estay M; Diaz-Valdes J
CS Departmento De Fisica Facultad de Ciencias Fisicas y Matematicas Universidad de Chile, Santiago..
SO MEDICAL HYPOTHESES, **(1989 Dec)** 30 (4) 265-9.
Journal code: M0M. ISSN: 0306-9877.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199005
AB The description of the **optimized** evolution of a code based on 4 nucleotides involves a sequential transition of codons, formed firstly by monomers evolving to dimers and then to triplets, in accordance with the progressive increase of the number of amino acids to be coded. The successive increase in the size of these codons during evolution implies changes in the phase reading of the genetic message, which could become chaotic. In order to overcome this constraint, this paper proposes a codon evolution where two things occur simultaneously: codons change in size and there is an alternation of the molecule which holds the information. For example, the nucleotides of the original oligonucleotide are read as monomers when they are translated to an oligopeptide, but further on, this oligopeptide which is read as amino acid dimers, is translated to a nucleotide form (oligonucleotide). Finally, amino acids conforming a peptide are translated from this oligonucleotide, through a reading of triplets. Although plausible, this evolution is a low-probability process due to the fact that it requires a singular sequence of the

oligonucleotide and oligopeptide involved. An alternative hypothesis of evolution is also discussed. It proposes that with the exclusion of the establishment of monomer and dimer codons, there is a direct generation of a code of trinucleotides which arises only when a certain number of amino acids has already been generated. Both hypotheses are discussed in terms of the development of a code in which an **optimized** hardware is maintained through out its evolution.
CT Check Tags: Support, Non-U.S. Gov't
Amino Acids: GE, genetics
***Codon: GE, genetics**
*Evolution
*Genetic Code
Models, Genetic
Oligodeoxyribonucleotides: GE, genetics
***RNA, Messenger: GE, genetics**
Translation, Genetic
CN 0 (Amino Acids); 0 (Codon); 0 (Oligodeoxyribonucleotides); 0 (**RNA**, Messenger)

L134 ANSWER 68 OF 126 MEDLINE
AN 90121889 MEDLINE
DN 90121889
TI Contextual constraints on codon pair usage: structural and biological implications.
AU Kolaskar A S; Reddy B V
CS Centre for Cellular and Molecular Biology, Hyderabad, India..
SO JOURNAL OF BIOMOLECULAR STRUCTURE AND DYNAMICS, **(1986 Feb)** 3 (4) 725-38.
Journal code: AH2. ISSN: 0739-1102.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199005
AB Complementary DNA sequence data of 278 protein coding genes from prokaryotic systems have been analysed at the level of near neighbour codon pairs. Our analysis points out that constraints exist even at the level of near neighbour codon pairs. These constraints are in addition to those which arise due to relative levels of tRNA. Codon pairs, which in the data base have different occurrence values from their expected values, neither have common secondary structure nor do have better **stabilization** due to high base stacking. Our study points out that there are strong interaction between constituent codons in these codon pairs. These strongly interacting codon pairs, we suggest, are involved in the formation of three dimensional structural elements of cDNA/**mRNA** and interact with ribosome and thus modulate translation.
CT Check Tags: Support, Non-U.S. Gov't
Base Sequence
***Codon: GE, genetics**
DNA: GE, genetics
Molecular Structure
***RNA, Messenger: GE, genetics**
Thermodynamics
RN 9007-49-2 (DNA)
CN 0 (Codon); 0 (**RNA**, Messenger)

L134 ANSWER 69 OF 126 MEDLINE
AN 90110051 MEDLINE
DN 90110051
TI Human thymidylate synthase gene: isolation of phage clones which cover a functionally active gene and structural analysis of the region upstream from the translation initiation codon.
AU Takeishi K; Kaneda S; Ayusawa D; Shimizu K; Gotoh O; Seno T
CS Department of Immunology and Virology, Saitama Cancer Center Research Institute.
SO JOURNAL OF BIOCHEMISTRY, **(1989 Oct)** 106 (4) 575-83.

Journal code: HIF. ISSN: 0021-924X.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199004
AB Two genomic DNA fragments partially encoding human thymidylate synthase (TS) [EC 2.1.1.45] were previously cloned in lambda phage from the mouse cell transformant, but had no transforming activity on mouse TS-negative mutant cells. In this study, an additional genomic DNA for human TS was cloned and demonstrated to have the transforming activity in combination with one of the two previously cloned DNAs and to produce human TS **mRNA**. The two transforming genomic DNAs overlapped and covered a region of 23 kb in total. Using fragments from one of these DNAs, the structure of the 1.2-kb region around the ATG initiator codon of the TS gene was analyzed in relation to regulatory sequences of the gene. Sequence determination demonstrated the presence of an unusual inverted repeat consisting of a triple tandem repeat of a 28-bp sequence and an inverted sequence of the same length. These sequences can form three possible, **stable**, stem-loop structures, which may be interconvertible. Based on S1 nuclease mapping data and a line of circumstantial evidence, we deduced two major **mRNA** cap sites within the inverted sequence. Comparison of the human and mouse sequences upstream from the ATG initiator codon revealed many significant blocks of sequence homology, especially in the regions around the deduced cap sites.
CT Check Tags: Animal; Human; Support, Non-U.S. Gov't
*Bacteriophage lambda: EN, enzymology
Base Sequence
Blotting, Northern
Cloning, Molecular
***Codon**
DNA, Viral: AN, analysis
DNA, Viral: GE, genetics
*Genes, Viral
Mice
Molecular Sequence Data
Peptide Chain Initiation
***RNA, Messenger**
**RNA, Viral: AN, analysis**
**RNA, Viral: GE, genetics**
*Thymidylate Synthase: GE, genetics
Transformation, Genetic
Translation, Genetic
CN EC 2.1.1.45 (Thymidylate Synthase); 0 (Codon); 0 (DNA, Viral); 0 (**RNA**, Messenger); 0 (**RNA**, Viral)

L134 ANSWER 70 OF 126 MEDLINE
AN 90101372 MEDLINE
DN 90101372
TI Changing the start codon context of the 30K gene of tobacco mosaic virus from "weak" to "strong" does not increase expression.
AU Lehto K; Dawson W O
CS Department of Plant Pathology, University of California, Riverside 92521..
SO VIROLOGY, **(1990 Jan)** 174 (1) 169-76.
Journal code: XEA. ISSN: 0042-6822.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199004
AB The translation initiation region of the 30K gene of tobacco mosaic virus (TMV) was modified by in vitro mutagenesis to create more **optimal** start codon contexts. A complicating factor was that modifications in this region also altered the 3' terminus of the 183K ORF that overlaps the 30K ORF. An insertion of GACUCGA between nucleotides 4901 and 4902 resulted in a purine (G) in position -3 relative to the AUG creating a "stronger"

start codon context, but this also changed the last four amino acids of the 183K protein. This mutant was infectious, replicated efficiently, but produced reduced amounts of 30K protein. Despite the reduced amount of movement protein, this mutant spread effectively from cell to cell and had a phenotype indistinguishable from that of wild-type virus. A more conservative mutation inserted GAC between TMV nucleotides 4901 and 4902 resulting in a "strong" start codon context (ACGAUGG) and modification of the 183K protein only by insertion of an aspartic acid adjacent to a native aspartic acid. This modification did not enhance the production of 30K protein. These data demonstrate consensus sequences that are **optimal** for other eukaryotic systems did not cause increased expression of the 30K gene in vivo. The modified sequences of both mutants were **stably** maintained during relatively long periods of replication. Even though each mutant replicated efficiently, when mixed with wild-type TMV, neither mutant effectively competed with the wild-type virus. Another mutant which removed the native 30K AUG to determine whether subsequent internal start codons with "stronger" contexts would function in its absence was constructed. However, this mutant and a mutant that fused the 183K reading frame to the 30K reading frame did not replicate and move in intact plants.

CT Check Tags: Support, U.S. Gov't, Non-P.H.S.
Base Sequence
Blotting, Western
***Codon: GE, genetics**
*Gene Expression Regulation, Viral
Molecular Sequence Data
Mutation
***RNA, Messenger: GE, genetics**
***RNA, Viral: GE, genetics**
*Tobacco Mosaic Virus: GE, genetics
Tobacco Mosaic Virus: PH, physiology
Transcription, Genetic
Translation, Genetic
Virus Replication

CN 0 (Codon); 0 (**RNA**, Messenger); 0 (**RNA**, Viral)

L134 ANSWER 71 OF 126 MEDLINE
AN 90098861 MEDLINE
DN 90098861
TI Expression of tetanus toxin fragment C in E. coli: high level expression by removing rare codons.
AU Makoff A J; Oxer M D; Romanos M A; Fairweather N F; Ballantine S
CS Department of Molecular Biology, Wellcome Biotech, Beckenham, Kent, UK.
SO NUCLEIC ACIDS RESEARCH, **(1989 Dec 25)** 17 (24) 10191-202.
Journal code: O8L. ISSN: 0305-1048.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199004
AB Tetanus toxin fragment C had been previously expressed in Escherichia coli at 3-4% cell protein. The codon bias for tetanus toxin in Clostridium tetani is very different from that of highly expressed homologous genes in E. coli, resulting in the presence of many rare E. coli codons in the sequence encoding fragment C. We have replaced the coding sequence by sequence **optimized** for codon usage in E. coli, and show that the expression of fragment C is increased. Although the level of **mRNA** also increased this appeared to be a secondary consequence of more efficient translation. Complete sequence replacement increased expression to approximately 11-14% cell protein but only after the promoter strength had been improved.

CT Amino Acid Sequence
Base Sequence
Cloning, Molecular
***Codon**
*Escherichia coli: GE, genetics

*Gene Expression
Molecular Sequence Data
Nucleic Acid Hybridization
*Peptide Fragments: GE, genetics
Plasmids
Promoter Regions (Genetics)
***RNA, Messenger**
**RNA, Messenger: GE, genetics**
*Tetanus Toxin: GE, genetics
Transcription, Genetic
CN 0 (tetanus toxin fragment C); 0 (Codon); 0 (Peptide Fragments); 0 (Plasmids); 0 (**RNA**, Messenger); 0 (Tetanus Toxin)

L134 ANSWER 72 OF 126 MEDLINE
AN 90066342 MEDLINE
DN 90066342
TI Context specific misreading of phenylalanine codons.
AU Precup J; Ulrich A K; Roopnarine O; Parker J
CS Department of Microbiology, Southern Illinois University, Carbondale 62901.
NC GM25855 (NIGMS)
SO MOLECULAR AND GENERAL GENETICS, **(1989 Sep)** 218 (3) 397-401.
Journal code: NGP. ISSN: 0026-8925.
CY GERMANY, WEST: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199003
AB It has previously been shown that the phenylalanine codon UUC encoding residue 8 of the Escherichia coli argI gene product, ornithine transcarbamylase, is misread as leucine at a high frequency during phenylalanine starvation. However, no misreading of the UUU encoding residue 3 was observed under these conditions. Using oligonucleotide-directed, site-specific mutagenesis, we have constructed mutants where these codons have been changed. Using these mutant argI genes we see a high level of mistranslation at position 8 during phenylalanine starvation whether the codon is UUU or UUC. With either codon at position 3 we see no leucine substitution. We also constructed a gene with a leucine codon at position 3. The product of this latter mutated gene is **stable** and active, indicating that preferential turnover of mistranslated protein is not obscuring an otherwise high rate of misreading. This would seem to indicate that it is the context rather than the particular phenylalanine codon which is important in determining these misreading levels.
CT Check Tags: Support, U.S. Gov't, P.H.S.
Amino Acid Sequence
Base Sequence
***Codon**
*Escherichia coli: GE, genetics
Molecular Sequence Data
Ornithine Carbamoyltransferase: GE, genetics
*Phenylalanine: GE, genetics
Plasmids
Restriction Mapping
***RNA, Messenger**
Translation, Genetic
RN 3617-44-5 (Phenylalanine)
CN EC 2.1.3.3 (Ornithine Carbamoyltransferase); 0 (Codon); 0 (Plasmids); 0 (**RNA**, Messenger)

L134 ANSWER 73 OF 126 MEDLINE
AN 90037070 MEDLINE
DN 90037070
TI Single base mutation in the type III procollagen gene that converts the codon for glycine 883 to aspartate in a mild variant of Ehlers-Danlos syndrome IV.
AU Tromp G; Kuivaniemi H; Stolle C; Pope F M; Prockop D J

CS Department of Biochemistry and Molecular Biology, Jefferson Institute of Molecular Medicine, Jefferson Medical College, Thomas Jefferson University, Philadelphia, Pennsylvania 19107.
NC AR-38188 (NIAMS)
SO JOURNAL OF BIOLOGICAL CHEMISTRY, **(1989 Nov 15)** 264 (32) 19313-7.
Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199002
AB Experiments were carried out to test the hypothesis that a 19-year-old proband with a mild variant of Ehlers-Danlos syndrome type IV had a mutation in the gene for type III procollagen. cDNA and genomic DNA were analyzed by using the polymerase chain reaction and cloning of the products into M13 filamentous phage. A mutation was found that converted the codon for glycine 883 of the triple-helical domain in one allele for type III procollagen to a codon for aspartate. The polymerase chain reaction introduced a few artifactual single base substitutions. Also, it was difficult to distinguish copies from the two alleles in many of the M13 clones. Therefore, several different strategies and analyses of about 50,000 nucleotide sequences in a series of clones were used to demonstrate that the mutation in the codon for glycine 883 was the only mutation in coding sequences for the triple-helical domain of type III procollagen that could have contributed to the phenotype. The same mutation in the codon for glycine 883 in one allele for type III procollagen was found in the proband's 52-year-old father who also had a mild variant of Ehlers-Danlos syndrome type IV. The type III procollagen synthesized by the proband's fibroblasts was analyzed by polyacrylamide gel electrophoresis. Less type III procollagen was secreted by the proband's fibroblasts than by control fibroblasts. Also, the thermal **stability** of the type III procollagen synthesized by the proband's fibroblasts was lower than the thermal **stability** of normal type III procollagen as assayed by brief protease digestion. The results, therefore, demonstrated that the single base mutation that converted the codon of glycine 883 to a codon for aspartate destabilized the entire triple helix of type III procollagen and probably accounted for the mild phenotype of Ehlers-Danlos syndrome type IV seen in the proband and her father.
CT Check Tags: Case Report; Female; Human; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Adult
*Aspartic Acid
Base Sequence
***Codon: GE, genetics**
DNA: GE, genetics
DNA-Directed DNA Polymerase
*Ehlers-Danlos Syndrome: GE, genetics
Fibroblasts: ME, metabolism
*Genes, Structural
*Glycine
Middle Age
Molecular Sequence Data
*Mutation
Polymerase Chain Reaction
*Procollagen: GE, genetics
Restriction Mapping
***RNA, Messenger: GE, genetics**
Skin: ME, metabolism
Templates
*Variation (Genetics)
RN 56-40-6 (Glycine); 56-84-8 (Aspartic Acid); 9007-49-2 (DNA)
CN EC 2.7.7.7 (DNA-Directed DNA Polymerase); 0 (Codon); 0 (Procollagen); 0 (**RNA**, Messenger)

L134 ANSWER 74 OF 126 MEDLINE

AN 90013326 MEDLINE
DN 90013326
TI Genetic code development by stop codon takeover.
AU Lehman N; Jukes T H
CS Space Sciences Laboratory, University of California, Berkeley, Oakland 94608..
SO JOURNAL OF THEORETICAL BIOLOGY, **(1988 Nov 21)** 135 (2) 203-14.
Journal code: K8N. ISSN: 0022-5193.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199001
AB A novel theoretical consideration of the origin and evolution of the genetic code is presented. Code development is viewed from the perspective of simultaneously evolving codons, anticodons and amino acids. Early code structure was determined primarily by thermodynamic **stability** considerations, requiring simplicity in primordial codes. More advanced coding stages could arise as biological systems became more complex and precise in their replication. To be consistent with these ideas, a model is described in which codons become permanently associated with amino acids only when a codon-anticodon pairing is strong enough to permit rapid translation. Hence all codons are essentially chain-termination or "stop" codons until tRNA adaptors evolve having the ability to bind tightly to them. This view, which draws support from several lines of evidence, differs from the prevalent thinking on code evolution which holds that codons specifying newer amino acids were derived from codons encoding older amino acids.
CT Check Tags: Human
Amino Acids: GE, genetics
***Codon**
DNA: GE, genetics
*Evolution
*Genetic Code
*Models, Genetic
**RNA: GE, genetics**
***RNA, Messenger**
RN **63231-63-0 (RNA)**; 9007-49-2 (DNA)
CN 0 (Amino Acids); 0 (Codon); 0 (**RNA**, Messenger)

L134 ANSWER 75 OF 126 MEDLINE
AN 89364726 MEDLINE
DN 89364726
TI Aminoglycoside suppression at UAG, UAA and UGA codons in Escherichia coli and human tissue culture cells.
AU Martin R; Mogg A E; Heywood L A; Nitschke L; Burke J F
CS Biochemistry Laboratory, University of Sussex, Falmer, UK.
SO MOLECULAR AND GENERAL GENETICS, **(1989 Jun)** 217 (2-3) 411-8.
Journal code: NGP. ISSN: 0026-8925.
CY GERMANY, WEST: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198912
AB We have compared the suppression of nonsense mutations by aminoglycoside antibiotics in Escherichia coli and in human 293 cells. Six nonsense alleles of the chloramphenicol acetyl transferase (cat) gene, in the vector pRSVcat, were suppressed by growth in G418 and paromomycin. Readthrough at UAG, UAA and UGA codons was monitored with enzyme assays for chloramphenicol acetyl transferase (CAT), in **stably** transformed bacteria and during transient expression from the same plasmid in human 293 tissue culture cells. We have found significant differences in the degree of suppression amongst three UAG codons and two UAA codons in different **mRNA** contexts. However, the pattern of these effects are not the same in the two organisms. Our data suggest that context effects of nonsense suppression may operate under different rules

in E. coli and human cells.
CT Check Tags: Comparative Study; Human; Support, Non-U.S. Gov't
Alleles
Amino Acid Sequence
*Aminoglycosides: PD, pharmacology
Base Sequence
Cell Line, Transformed
Chloramphenicol O-Acetyltransferase: GE, genetics
**Codon: DE, drug effects**
***Codon: GE, genetics**
Escherichia coli: GE, genetics
Molecular Sequence Data
Mutation
**RNA, Bacterial: DE, drug effects**
**RNA, Bacterial: GE, genetics**
***RNA, Messenger: GE, genetics**
*Suppression, Genetic: DE, drug effects
CN EC 2.3.1.28 (Chloramphenicol O-Acetyltransferase); 0 (Aminoglycosides); 0 (Codon); 0 (**RNA**, Bacterial); 0 (**RNA**, Messenger)

L134 ANSWER 76 OF 126 MEDLINE
AN 89345068 MEDLINE
DN 89345068
TI Codon usage and gene expression level in Dictyostelium discoideum: highly expressed genes do 'prefer' **optimal** codons.
AU Sharp P M; Devine K M
CS Department of Genetics, Trinity College, Dublin, Ireland..
SO NUCLEIC ACIDS RESEARCH, **(1989 Jul 11)** 17 (13) 5029-39.
Journal code: O8L. ISSN: 0305-1048.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198911
AB Codon usage patterns in the slime mould Dictyostelium discoideum have been re-examined (a total of 58 genes have been analysed). Considering the extreme A + T-richness of this genome (G + C = 22%), there is a surprising degree of codon usage variation among genes. For example, G + C content at silent sites varies from less than 10% to greater than 30%. It was previously suggested [Warrick, H.M. and Spudich, J.A. (1988) Nucleic Acids Res. 16: 6617-6635] that highly expressed genes contain fewer '**optimal**' codons than genes expressed at lower levels. However, it appears that the **optimal** codons were misidentified. Multivariate statistical analysis shows that the greatest variation among genes is in relative usage of a particular subset of codons (about one per amino acid), many of which are C-ending. We have identified these as **optimal** codons, since (i) their frequency is positively correlated with gene expression level, and (ii) there is a strong mutation bias in this genome towards A and T nucleotides. Thus, codon usage in D. discoideum can be explained by a balance between the forces of mutational bias and translational selection.
CT Check Tags: Support, Non-U.S. Gov't
***Codon: GE, genetics**
*Dictyostelium: GE, genetics
*Genes, Fungal
Genes, Structural
Information Systems
***RNA, Messenger: GE, genetics**
*Transcription, Genetic
CN 0 (Codon); 0 (**RNA**, Messenger)

L134 ANSWER 77 OF 126 MEDLINE
AN 89342454 MEDLINE
DN 89342454
TI Novel third-letter bias in Escherichia coli codons revealed by rigorous treatment of coding constraints.

AU Hanai R; Wada A
CS Department of Physics, Faculty of Science, University of Tokyo, Japan..
SO JOURNAL OF MOLECULAR BIOLOGY, **(1989 Jun 20)** 207 (4) 655-60.
Journal code: J6V. ISSN: 0022-2836.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198911
AB A novel bias in codon third-letter usage was found in Escherichia coli genes with low fractions of "**optimal** codons", by comparing intact sequences with control random sequences. Third-letter usage has been found to be biased according to preference in codon usage and to doublet preference from the following first letter. The present study examines third-letter usage in the context of the nucleotide sequence when these preferences are considered. In order to exclude any influence by these factors, the random sequences were generated such that the amino acid sequence, codon usage, and the doublet frequency in each gene were all preserved. Comparison of intact sequences with these randomly generated sequences reveals that third letters of codons show a strong preference for the purine/pyrimidine pattern of the next codons: purine (R) is preferred to pyrimidine (Y) at the third site when followed by an R-Y-R codon, and pyrimidine is preferred when followed by an R-R-Y, an R-Y-Y or a Y-R-Y codon. This bias is probably related to interactions of tRNA molecules in the ribosome.
CT Check Tags: Support, Non-U.S. Gov't
Amino Acids: GE, genetics
Base Sequence
***Codon**
*Escherichia coli: GE, genetics
Methods
Purine Nucleotides
Pyrimidine Nucleotides
**RNA, Bacterial: GE, genetics**
***RNA, Messenger**
CN 0 (Amino Acids); 0 (Codon); 0 (Purine Nucleotides); 0 (Pyrimidine Nucleotides); 0 (**RNA**, Bacterial); 0 (**RNA**, Messenger)

L134 ANSWER 78 OF 126 MEDLINE
AN 89329029 MEDLINE
DN 89329029
TI Codon usage determines translation rate in Escherichia coli.
AU Sorensen M A; Kurland C G; Pedersen S
CS Institute of Microbiology, University of Copenhagen, Denmark..
SO JOURNAL OF MOLECULAR BIOLOGY, **(1989 May 20)** 207 (2) 365-77.
Journal code: J6V. ISSN: 0022-2836.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198911
AB We wish to determine whether differences in translation rate are correlated with differences in codon usage or with differences in **mRNA** secondary structure. We therefore inserted a small DNA fragment in the lacZ gene either directly or flanked by a few frame-shifting bases, leaving the reading frame of the lacZ gene unchanged. The fragment was chosen to have "infrequent" codons in one reading frame and "common" codons in the other. The insert in these constructs does not seem to give **mRNAs** that are able to form extensive secondary structures. The translation time for these modified lacZ **mRNAs** was measured with a reproducibility better than plus or minus one second. We found that the **mRNA** with infrequent codons inserted has an approximately three-seconds longer translation time than the one with common codons. In another set of experiments we constructed two almost identical lacZ genes in which the lacZ **mRNAs** have the potential to generate stem structures with

**stabilities** of about -75 kcal/mol. In this way we could investigate the influence of **mRNA** structure on translation rate. This type of modified gene was generated in two reading frames with either common or infrequent codons similar to our first experiments. We find that the yield of protein from these **mRNAs** is reduced, probably due to the action in vivo of an RNase. Nevertheless, the data do not indicate that there is any effect of **mRNA** secondary structure on translation rate. In contrast, our data persuade us that there is a difference in translation rate between infrequent codons and common codons that is of the order of sixfold.

CT Check Tags: Support, Non-U.S. Gov't
Bacterial Proteins: AN, analysis
Base Sequence
***Codon**
*Escherichia coli: GE, genetics
Lac Operon
Molecular Sequence Data
Nucleic Acid Conformation
**RNA, Bacterial: GE, genetics**
***RNA, Messenger**
**RNA, Messenger: GE, genetics**
Time Factors
*Translation, Genetic

CN 0 (Bacterial Proteins); 0 (Codon); 0 (**RNA**, Bacterial); 0 (**RNA**, Messenger)

L134 ANSWER 79 OF 126 MEDLINE
AN 89289712 MEDLINE
DN 89289712
TI Effect of spermine on the efficiency and fidelity of the codon-specific binding of tRNA to the ribosomes.
AU Naranda T; Kucan Z
CS Department of Chemistry, Faculty of Science, University of Zagreb, Jugoslavija..
SO EUROPEAN JOURNAL OF BIOCHEMISTRY, **(1989 Jun 15)** 182 (2) 291-7.
Journal code: EMZ. ISSN: 0014-2956.
CY GERMANY, WEST: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198910
AB Binding of the yeast Tyr-tRNA and Phe-tRNA to the A site, and the binding of their acetyl derivatives to the P site of poly(U11,A)-programmed Escherichia coli ribosomes was studied. Spermine stimulated the rate of binding of both tRNAs at least threefold, enabling more than 90% final saturation of both ribosomal binding sites. The effect is observed when the tRNAs, but not ribosomes or poly(U11,A), are preincubated with polyamine. Regardless of the binding site, **optimal** saturation was reached at spermine/tRNA molar ratios of 3 for tRNA(Phe) and 5 for tRNA(Tyr). The same low spermine/tRNA ratios were previously reported to **stabilize** the conformation of these tRNAs in solution. On the other hand, the messenger-free, EF-Tu- and EF-G-dependent polymerization of lysine from E. coli Lys-tRNA is drastically reduced, while the poly(A)-directed polymerization is stimulated by spermine through a wide range of Mg2+ concentrations. Misreading of UUU codons as isoleucine, assayed by the A-site binding of E. coli Ile-tRNA, is also inhibited by spermine. All these results demonstrate that spermine increases the efficiency and accuracy of a series of macromolecular interactions leading to the correct incorporation of an amino acid into protein, at the same time preventing some unspecific or erroneous interactions. From the analogy with its known structural effects, it can be inferred that spermine does so by conferring on the tRNA a specific biologically functional conformation.

CT Binding Sites
***Codon: ME, metabolism**
Escherichia coli: ME, metabolism

Poly U: ME, metabolism
***RNA, Messenger: ME, metabolism**
***RNA, Ribosomal: ME, metabolism**
***RNA, Transfer: ME, metabolism**
**RNA, Transfer, Phe: ME, metabolism**
**RNA, Transfer, Tyr: ME, metabolism**
*Spermine: PD, pharmacology
Time Factors
Yeasts: ME, metabolism
RN 27416-86-0 (Poly U); 71-44-3 (Spermine); **9014-25-9 (RNA, Transfer)**
CN 0 (Codon); 0 (**RNA**, Messenger); 0 (**RNA**, Ribosomal); 0 (**RNA**, Transfer, Phe); 0 (**RNA**, Transfer, Tyr)

L134 ANSWER 80 OF 126 MEDLINE
AN 89207718 MEDLINE
DN 89207718
TI On the information content of the genetic code.
AU Alvager T; Graham G; Hilleke R; Hutchison D; Westgard J
CS Physics Department, Indiana State University, Terre Haute 47809..
SO BIOSYSTEMS, **(1989)** 22 (3) 189-96. Ref: 13
Journal code: A6E. ISSN: 0303-2647.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 198908
AB In living organisms 20 amino acids along with the terminator value(s) are encoded by 64 codons giving a degeneracy of the codons as described by the genetic code. A basic theoretical problem of genetic codes is to explain the particular distribution of degeneracies of partitions involved in the codes. In this work the degeneracy problem is considered in the framework of information theory. It is shown by direct numerical evaluation of a certain degeneracy information function associated with the genetic code that the degeneracy of the codes is observed to be related to the **optimization** of this function.
CT Amino Acids: GE, genetics
***Codon: GE, genetics**
Data Interpretation, Statistical
*Genetic Code
Models, Genetic
***RNA, Messenger: GE, genetics**
CN 0 (Amino Acids); 0 (Codon); 0 (**RNA**, Messenger)

L134 ANSWER 81 OF 126 MEDLINE
AN 89127179 MEDLINE
DN 89127179
TI [Two-codon mutagenesis of alpha-amylase gene of Bacillus amyloliquefaciens].
Dvukhkodonnyi mutagenez gena alpha-amilazy Bacillus amyloliquefaciens.
AU Smirnova N A; Sorokin A V; Laptev D A; Veiko V P; Kozlov IuI
SO MOLEKULIARNAIA BIOLOGIIA, **(1988 Sep-Oct)** 22 (5) 1265-71.
Journal code: NGX. ISSN: 0026-8984.
CY USSR
DT Journal; Article; (JOURNAL ARTICLE)
LA Russian
FS Priority Journals
EM 198905
AB The oligonucleotide encoding Bam HI recognition site having the structure pCGGGATC had been inserted into the recognition sites MspI of the B. amyloliquefaciens alpha-amylase gene, which was cloned in pTG29B plasmid. The alpha-amylase gene had no BamHI sites before mutagenesis. The set of pNSBamHI plasmids with BamHI site at four different positions was obtained. It was shown that all the mutant alpha-amylases possess different specific activities. One of the mutant proteins possesses

reduced thermostability. The mutant alpha-amylases can be used for further experiments on protein-engineering of liquefying-type alpha-amylases.

CT *alpha-Amylase: GE, genetics
Bacillus: EN, enzymology
*Bacillus: GE, genetics
***Codon**
Deoxyribonucleases, Type II Site-Specific
English Abstract
**Enzyme Stability**
*Genes, Bacterial
Heat
*Mutation
Plasmids
Restriction Mapping
***RNA, Messenger**

CN EC 3.1.21.- (Deoxyribonuclease HpaII); EC 3.1.21.4 (Deoxyribonucleases, Type II Site-Specific); EC 3.2.1.1 (alpha-Amylase); 0 (Codon); 0 (Plasmids); 0 (**RNA**, Messenger)

L134 ANSWER 82 OF 126 MEDLINE
AN 89098942 MEDLINE
DN 89098942
TI Presence of the hypermodified nucleotide N6-(delta 2-isopentenyl)-2-methylthioadenosine prevents codon misreading by Escherichia coli phenylalanyl-transfer **RNA**.
AU Wilson R K; Roe B A
CS Department of Chemistry and Biochemistry, University of Oklahoma, Norman 73019.
NC GM30400 (NIGMS)
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, **(1989 Jan)** 86 (2) 409-13.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198904
AB The overall structure of transfer **RNA** is **optimized** for its various functions by a series of unique post-transcriptional nucleotide modifications. Since many of these modifications are conserved from prokaryotes through higher eukaryotes, it has been proposed that most modified nucleotides serve to **optimize** the ability of the tRNA to accurately interact with other components of the protein synthesizing machinery. When a cloned synthetic Escherichia coli tRNAPhe gene was transfected into a bacterial host that carried a defective phenylalanine tRNA-synthetase gene, tRNAPhe was overexpressed by 11-fold. As a result of this overexpression, an undermodified tRNAPhe species was produced that lacked only N6-(delta 2-isopentenyl)-2-methylthioadenosine (ms2i6A), a hypermodified nucleotide found immediately 3' to the anticodon of all major E. coli tRNAs that read UNN codons. To investigate the role of ms2i6A in E. coli tRNA, we compared the aminoacylation kinetics and in vitro codon-reading properties of the ms2i6A-lacking and normal fully modified tRNAPhe species. The results of these experiments indicate that while ms2i6A is not required for normal aminoacylation of tRNAPhe, its presence **stabilizes** codon-anticodon interaction and thereby prevents misreading of the genetic code.
CT Check Tags: Support, U.S. Gov't, P.H.S.
*Adenosine: AA, analogs & derivatives
Amino Acid Sequence
Base Sequence
Chromatography, Thin Layer
Cloning, Molecular
***Codon: GE, genetics**
*Escherichia coli: GE, genetics
Fractionation
Gene Expression Regulation

*Isopentenyladenosine: AA, analogs & derivatives
Isopentenyladenosine: GE, genetics
Isopentenyladenosine: ME, metabolism
Kinetics
Molecular Sequence Data
Phenylalanine-tRNA Ligase: GE, genetics
***RNA Processing, Post-Transcriptional**
***RNA, Messenger: GE, genetics**
***RNA, Transfer, Amino Acid-Specific: ME, metabolism**
**RNA, Transfer, Phe: BI, biosynthesis**
**RNA, Transfer, Phe: GE, genetics**
**RNA, Transfer, Phe: IP, isolation & purification**
***RNA, Transfer, Phe: ME, metabolism**
Transcription, Genetic
Translation, Genetic
RN 20859-00-1 (2-methylthio-N-6-isopentenyladenosine); 58-61-7 (Adenosine); 7724-76-7 (Isopentenyladenosine)
CN EC 6.1.1.20 (Phenylalanine-tRNA Ligase); 0 (Codon); 0 (**RNA**, Messenger); 0 (**RNA**, Transfer, Amino Acid-Specific); 0 (**RNA**, Transfer, Phe)

L134 ANSWER 83 OF 126 MEDLINE
AN 89094868 MEDLINE
DN 89094868
TI Specific codon usage pattern and its implications on the secondary structure of silk fibroin **mRNA**.
AU Mita K; Ichimura S; Zama M; James T C
CS Division of Chemistry, National Institute of Radiological Sciences, Chiba, Japan.
NC R01 GM30273 (NIGMS)
SO JOURNAL OF MOLECULAR BIOLOGY, **(1988 Oct 20)** 203 (4) 917-25. Journal code: J6V. ISSN: 0022-2836.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198904
AB We have identified two distinctive regions of the repetitive unit nucleotide sequence of fibroin **mRNA** of Bombyx mori. The codon usage for the major amino acids, glycine, alanine and serine is distinctly different in these two regions, indicating that it is determined by the fibroin **mRNA** or gene structure but not by the tRNA population. Comparative computer analyses of nucleotide substitutions in the unit sequence suggest that selection has operated on the codon usage to **optimize** the secondary structure characteristic of the fibroin **mRNA**.
CT Check Tags: Animal; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Amino Acid Sequence
***Codon**
Computer Simulation
DNA, Circular: GE, genetics
*Fibroin: GE, genetics
Genes
Molecular Sequence Data
*Repetitive Sequences, Nucleic Acid
***RNA, Messenger**
***RNA, Messenger: GE, genetics**
*Silkworms: GE, genetics
RN 9007-76-5 (Fibroin)
CN 0 (Codon); 0 (DNA, Circular); 0 (**RNA**, Messenger)

L134 ANSWER 84 OF 126 MEDLINE
AN 88330060 MEDLINE
DN 88330060
TI A substitution of cytosine for thymine in codon 110 of the human beta-globin gene is a novel cause of beta-thalassemia phenotypes.

AU Naritomi Y; Naito Y; Nakashima H; Yokota E; Imamura T
CS First Department of Medicine, Faculty of Medicine, Kyushu University, Fukuoka, Japan..
SO HUMAN GENETICS, **(1988 Sep)** 80 (1) 11-5.
Journal code: GED. ISSN: 0340-6717.
CY GERMANY, WEST: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198812
AB We have described a novel human globin gene mutation that produced in a Japanese family the beta-thalassemia phenotype through a post-translational mechanism. Substitution of proline for leucine at position 110 in the G-helix of the beta-globin chain greatly reduced the molecular **stability** of the beta-globin subunit, leading to total destruction of the variant globin chains by proteolysis and hence to the beta-thalassemia phenotype. The mutation could be identified after MspI digestion. This detection of the mutation on the gene level is valuable for diagnostic purposes.
CT Check Tags: Human; Support, Non-U.S. Gov't
Amino Acid Sequence
Base Sequence
***Codon**
*Cytosine
*Genes, Structural
*Globin: GE, genetics
Molecular Sequence Data
Phenotype
***RNA, Messenger**
Thalassemia: BL, blood
*Thalassemia: GE, genetics
*Thymine
RN 65-71-4 (Thymine); 71-30-7 (Cytosine); 9004-22-2 (Globin)
CN 0 (Codon); 0 (**RNA**, Messenger)

L134 ANSWER 85 OF 126 MEDLINE
AN 88299168 MEDLINE
DN 88299168
TI New amber mutation in a beta-thalassemic gene with nonmeasurable levels of mutant messenger **RNA** in vivo.
AU Atweh G F; Brickner H E; Zhu X X; Kazazian H H Jr; Forget B G
CS Department of Medicine, University of Michigan School of Medicine, Ann Arbor..
SO JOURNAL OF CLINICAL INVESTIGATION, **(1988 Aug)** 82 (2) 557-61.
Journal code: HS7. ISSN: 0021-9738.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 198811
AB We have identified a beta-thalassemia gene that carries a novel nonsense mutation in a Chinese patient. This mutation, a G to T substitution at the first position of codon 43, changes the glutamic acid coding triplet (GAG) to a terminator codon (TAG). Based on oligonucleotide hybridization studies of 78 Chinese and Southeast Asian beta-thalassemia chromosomes, we estimate that this mutation accounts for a small minority of the beta-thalassemia mutations in that population. Study of the expression of this cloned gene in a transient expression system demonstrated a 65% decrease in levels of normally spliced mutant beta-globin **mRNA**. However, the study of reticulocyte **RNA** isolated from an individual heterozygous for this mutation demonstrated a total absence of this mutant **mRNA** in vivo. The basis for this big discrepancy between the level of accumulated **mRNA** in vivo and in vitro is probably the result of differences in the **stabilities** of the mutant **mRNA** in erythroid cells.
CT Check Tags: Human; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't,

P.H.S.
Amino Acid Sequence
Base Sequence
***Codon: GE, genetics**
*Genes, Structural
Globin: GE, genetics
Molecular Sequence Data
*Mutation
Oligonucleotides: CS, chemical synthesis
Polymorphism (Genetics)
Reticulocytes: AN, analysis
***RNA, Messenger: GE, genetics**
***RNA, Messenger: IP, isolation & purification**
Thalassemia: BL, blood
*Thalassemia: GE, genetics
Transcription, Genetic
RN 9004-22-2 (Globin)
CN 0 (Codon); 0 (Oligonucleotides); 0 (**RNA**, Messenger)

L134 ANSWER 86 OF 126 MEDLINE
AN 88227821 MEDLINE
DN 88227821
TI Mutations in the leader sequence and initiation codon of the gene for ribosomal protein S20 (rpsT) affect both translational efficiency and autoregulation.
AU Parsons G D; Donly B C; Mackie G A
CS Department of Biochemistry, University of Western Ontario, London, Canada..
SO JOURNAL OF BACTERIOLOGY, **(1988 Jun)** 170 (6) 2485-92.
Journal code: HH3. ISSN: 0021-9193.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198809
AB We have transferred the complete structural gene and part of the leader for ribosomal protein S20 of Escherichia coli to a controllable expression vector and have used oligonucleotide-directed mutagenesis to create mutations in the untranslated leader of the plasmid-borne gene. We have assayed for posttranscriptional regulation of the synthesis of S20 after inducing transcription of the mutant S20 **mRNA** from the expression vector. We found that two mutations lead to loss of feedback control of S20 synthesis: (i) a change of the initiation codon from UUG to AUG and (ii) a replacement of part of the S20 leader with a nonhomologous sequence including an AUG initiation codon. These mutations also lead to increases in both the intrinsic translational efficiency of the plasmid-encoded S20 **mRNA** in vitro and its half-life in vivo. A double mutation (GA to CT) at residues -3 and -4 relative to the initiation codon does not result in overproduction of S20. Rather, it reduces translational efficiency in vitro and **mRNA stability** in vivo. Our results demonstrate the fundamental importance of the UUG initiation codon in mediating autogenous repression of S20 synthesis.
CT Check Tags: Support, Non-U.S. Gov't
Base Sequence
Cloning, Molecular
***Codon**
Escherichia coli: GE, genetics
Genes, Structural
*Mutation
*Peptide Chain Initiation
*Ribosomal Proteins: GE, genetics
***RNA, Messenger**
*Signal Peptides: GE, genetics
*Translation, Genetic
CN 0 (ribosomal protein S20); 0 (Codon); 0 (Ribosomal Proteins); 0 (

**RNA**, Messenger); 0 (Signal Peptides)

L134 ANSWER 87 OF 126 MEDLINE
AN 88155638 MEDLINE
DN 88155638
TI Codon distribution in vertebrate genes may be used to predict gene length.
AU Bains W
CS Department of Biochemistry, University of Bath, Claverton Down, England.
SO JOURNAL OF MOLECULAR BIOLOGY, **(1987 Oct 5)** 197 (3) 379-88.
Journal code: J6V. ISSN: 0022-2836.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198806
AB I have analysed the coding regions of 96 eukaryotic genes for their use of iso-coding codons. Specific codons occur more frequently in specific positions in all members of some gene families than would be expected if codon choice was determined solely by the frequency of codon usage. In the absence of evidence a priori for selection for particular codons at particular positions, I term such co-occurring codons "coincident codons". Coincident codons are not confined to particular regions of genes, and their occurrence is not detectably linked with the location of introns in the genomic sequence. Their presence is partly but not completely explained by the exchange of sequence between similar functional genes within a species: homologous genes from different organisms also possess the same codons at some sites with greater than expected frequencies. The relative excess of coincident codons correlates well with the overall length of the genes analysed, but not with the length of **mRNA** or coding regions, or with qualitative features of gene structure or expression. This, and the unusual sequence environment of coincident codons, suggests that they are a feature of the overall secondary structure of the heterogeneous nuclear **RNA**. Such considerations suggest approaches for **optimizing** the expression of exogenous genes in eukaryotic systems, and for predicting the structure of genes for which only partial sequence data is available.
CT Check Tags: Animal; Comparative Study; Support, Non-U.S. Gov't
Actins: GE, genetics
Base Sequence
***Codon**
*Genes, Structural
Multigene Family
***RNA, Messenger**
Sequence Homology, Nucleic Acid
Vertebrates: GE, genetics
CN 0 (Actins); 0 (Codon); 0 (**RNA**, Messenger)

L134 ANSWER 88 OF 126 MEDLINE
AN 88107877 MEDLINE
DN 88107877
TI Decoding at the ribosomal A site: antibiotics, misreading and energy of aminoacyl-tRNA binding.
AU Hornig H; Woolley P; Luhrmann R
CS Max-Planck-Institut fur molekulare Genetik, Berlin, F.R.G..
SO BIOCHIMIE, **(1987 Aug)** 69 (8) 803-13.
Journal code: A14. ISSN: 0300-9084.
CY France
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198805
AB The binding of Phe-tRNAPhe at the programmed ribosomal A site has been investigated using antibiotics that influence this binding in different ways. The adhesion of Phe-tRNAPhe, the consumption of GTP and the extent of the peptidyl transfer reaction were monitored. All of the five known misreading-inducing antibiotics that were tested **stabilised** the

binding of Phe-tRNAPhe after its affixture to the A site by EF-Tu with GTP hydrolysis. The **stabilisation** was sufficient to overcome a single mismatch in the codon-anticodon interaction. Combinations of **stabilising** and destabilising influences were found to be additive, thus supporting the concepts: (1) that there is a 'correct' binding energy for aminoacyl tRNA in the A site, whose reduction hampers polypeptide synthesis and whose increase makes it inaccurate by by-passing proofreading; and (2) that the different antibiotics affect the bound aminoacyl tRNA at different points.

CT *Antibiotics: PD, pharmacology
***Codon**
Escherichia coli: ME, metabolism
Peptides: ME, metabolism
Ribosomes: DE, drug effects
*Ribosomes: ME, metabolism
***RNA, Messenger**
***RNA, Transfer, Amino Acid-Specific: ME, metabolism**
*Translation, Genetic: DE, drug effects

CN 0 (Antibiotics); 0 (Codon); 0 (Peptides); 0 (**RNA**, Messenger); 0 (**RNA**, Transfer, Amino Acid-Specific)

L134 ANSWER 89 OF 126 MEDLINE
AN 88062727 MEDLINE
DN 88062727
TI At least six nucleotides preceding the AUG initiator codon enhance translation in mammalian cells.
AU Kozak M
CS Department of Biological Sciences, University of Pittsburgh, PA 15260.
NC GM33915 (NIGMS)
SO JOURNAL OF MOLECULAR BIOLOGY, **(1987 Aug 20)** 196 (4) 947-50.
Journal code: J6V. ISSN: 0022-2836.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Cancer Journals; Priority Journals
EM 198803
AB Sequences flanking the AUG initiator codon influence its recognition by eukaryotic ribosomes. From a comparison of several hundred **mRNA** sequences, CCA/GCCAUGG emerged as the consensus sequence for initiation in higher eukaryotes. Systematic mutagenesis of a cloned preproinsulin gene confirmed the facilitating effect of A or G in position -3 (i.e. 3 nucleotides upstream from the AUG codon), C in positions -1 and -2, and G immediately following the AUG codon. The analysis of a new set of mutants now reveals that sequences slightly farther upstream are also influential, the **optimal** context for initiation being (GCC)GCCA/GCCAUGG. Possible mechanistic implications of the repeating GCC motif are discussed.
CT Check Tags: Support, U.S. Gov't, P.H.S.
Base Sequence
***Codon**
Mutation
Proinsulin: GE, genetics
Protein Precursors: GE, genetics
***RNA, Messenger**
*Translation, Genetic
RN 61116-24-3 (preproinsulin); 9035-68-1 (Proinsulin)
CN 0 (Codon); 0 (Protein Precursors); 0 (**RNA**, Messenger)

L134 ANSWER 90 OF 126 MEDLINE
AN 88038832 MEDLINE
DN 88038832
TI Codon replacement in the PGK1 gene of Saccharomyces cerevisiae: experimental approach to study the role of biased codon usage in gene expression.
AU Hoekema A; Kastelein R A; Vasser M; de Boer H A
CS Department of Cell Genetics, Genentech, Inc., South San Francisco,

California 94080..
SO MOLECULAR AND CELLULAR BIOLOGY, **(1987 Aug)** 7 (8) 2914-24.
Journal code: NGY. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-M17195
EM 198802
AB The coding sequences of genes in the yeast Saccharomyces cerevisiae show a preference for 25 of the 61 possible coding triplets. The degree of this biased codon usage in each gene is positively correlated to its expression level. Highly expressed genes use these 25 major codons almost exclusively. As an experimental approach to studying biased codon usage and its possible role in modulating gene expression, systematic codon replacements were carried out in the highly expressed PGK1 gene. The expression of phosphoglycerate kinase (PGK) was studied both on a high-copy-number plasmid and as a single copy gene integrated into the chromosome. Replacing an increasing number (up to 39% of all codons) of major codons with synonymous minor ones at the 5' end of the coding sequence caused a dramatic decline of the expression level. The PGK protein levels dropped 10-fold. The steady-state **mRNA** levels also declined, but to a lesser extent (threefold). Our data indicate that this reduction in **mRNA** levels was due to destabilization caused by impaired translation elongation at the minor codons. By preventing translation of the PGK **mRNAs** by the introduction of a stop codon 3' and adjacent to the start codon, the steady-state **mRNA** levels decreased dramatically. We conclude that efficient **mRNA** translation is required for maintaining **mRNA stability** in S. cerevisiae. These findings have important implications for the study of the expression of heterologous genes in yeast cells.
CT Amino Acid Sequence
Base Sequence
***Codon**
DNA Restriction Enzymes
DNA, Recombinant: ME, metabolism
*Genes, Fungal
*Genes, Structural
*Phosphoglycerate Kinase: GE, genetics
Plasmids
***RNA, Messenger**
Saccharomyces cerevisiae: EN, enzymology
*Saccharomyces cerevisiae: GE, genetics
*Transcription, Genetic
CN EC 2.7.2.3 (Phosphoglycerate Kinase); EC 3.1.21 (DNA Restriction Enzymes); 0 (Codon); 0 (DNA, Recombinant); 0 (Plasmids); 0 (**RNA,** Messenger)

L134 ANSWER 91 OF 126 MEDLINE
AN 88013826 MEDLINE
DN 88013826
TI [Affinity modification of Escherichia coli ribosomes by 4-[(N-2-chloroethyl)N-methylamino]benzyl-5'-phosphamide hexauridylate in a complex **stabilized** by codon-anticodon interactions on P and A sites].
Affinnaia modifikatsiia ribosom Escherichia coli 4-[(N-2-khloretil)N-metilamino]benzil-5'-fosfamidom geksauridilata v komplekse, **stabiliziruemom** kodon-antikodonovym vzaimodeistviem v P- i A-uchastke.
AU Gimautdinova O I; Karpova G G
SO MOLEKULIARNAIA BIOLOGIIA, **(1987 Jul-Aug)** 21 (4) 942-8.
Journal code: NGX. ISSN: 0026-8984.
CY USSR
DT Journal; Article; (JOURNAL ARTICLE)
LA Russian
FS Priority Journals

EM 198801
AB Affinity labeling of E. coli ribosomes with 4-[(N-2-chloroethyl)-N-methylamino] benzyl-5'-phosphamide of hexauridylate was studied within the complex containing tRNAPhe at P site and Phe-tRNAPhe at A site directed by EF-Tu and GTP. Ribosomal proteins as well as rRNA both in 30S and 50S subunits were found to be labelled within the complex. Labeled proteins were identified as S3, S9 and L2. Selectivity of affinity labeling with **mRNA** analogs was shown to depend on the functional state of the ribosomes. Modification was more selective within the complex **stabilized** by codon-anticodon interaction both at A and P-sites than within the complex in which this interaction takes place preferentially at P site.
CT ***Anticodon**
***Codon**
Electrophoresis, Polyacrylamide Gel
English Abstract
Escherichia coli: GE, genetics
*Escherichia coli: ME, metabolism
Organometallic Compounds: ME, metabolism
*Organometallic Compounds: PD, pharmacology
Ribosomal Proteins: ME, metabolism
*Ribosomes: ME, metabolism
***RNA, Messenger**
**RNA, Ribosomal: ME, metabolism**
***RNA, Transfer**
**RNA, Transfer, Phe: ME, metabolism**
*Uracil Nucleotides: PD, pharmacology
Uridine Monophosphate: AA, analogs & derivatives
Uridine Monophosphate: ME, metabolism
*Uridine Monophosphate: PD, pharmacology
RN 58-97-9 (Uridine Monophosphate); **9014-25-9 (RNA, Transfer)**
CN 0 (Anticodon); 0 (Codon); 0 (Organometallic Compounds); 0 (Ribosomal Proteins); 0 (**RNA**, Messenger); 0 (**RNA**, Ribosomal); 0 (**RNA**, Transfer, Phe); 0 (Uracil Nucleotides)

L134 ANSWER 92 OF 126 MEDLINE
AN 88011313 MEDLINE
DN 88011313
TI Destabilization of codon-anticodon interaction in the ribosomal exit site.
AU Lill R; Wintermeyer W
CS Institut fur Physiologische Chemie, Physikalische Biochemie und Zellbiologie, Universitat Munchen, F.R.G..
SO JOURNAL OF MOLECULAR BIOLOGY, **(1987 Jul 5)** 196 (1) 137-48.
Journal code: J6V. ISSN: 0022-2836.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198801
AB The affinities of the exit (E) site of poly(U) or poly(A)-programmed Escherichia coli ribosomes for the respective cognate tRNA and a number of non-cognate tRNAs were determined by equilibrium titrations. Among the non-cognate tRNAs, the binding constants vary up to about tenfold (10(6) to 10(7) M-1 at 20 mM-Mg2+) or 50-fold (10 mM-Mg2+), indicating that codon-independent binding is modulated to a considerable extent by structural elements of the tRNA molecules other than the anticodon. Codon-anticodon interaction **stabilizes** tRNA binding in the E site approximately fourfold (20 mM-Mg2+) or 20-fold (10 mM-Mg2+), corresponding to delta G degree values of -3 and -7 kJ/mol (0.7 and 1.7 kcal/mol), respectively. Thus, the energetic contribution of codon-anticodon interaction to tRNA binding in the E site appears rather small, particularly in comparison to the large effects on the binding in A and P sites and to the binding of complementary oligonucleotides or of tRNAs with complementary anticodons. This result argues against a role of the E site-bound tRNA in the fixation of the **mRNA** on the ribosome. In contrast, we propose that the role of the E site is to

facilitate the release of the discharged tRNA during translocation by providing an intermediate, labile binding site for the tRNA leaving the P site. The lowering of both affinity and **stability** of tRNA binding accompanying the transfer of the tRNA from the P site to the E site is predominantly due to the labilization of the codon-anticodon interaction.

CT Check Tags: Support, Non-U.S. Gov't
***Anticodon: ME, metabolism**
Binding Sites
***Codon: ME, metabolism**
Escherichia coli: ME, metabolism
*Ribosomes: ME, metabolism
**RNA, Bacterial: ME, metabolism**
***RNA, Messenger: ME, metabolism**
***RNA, Transfer: ME, metabolism**
**RNA, Transfer, Amino Acyl: ME, metabolism**
Spectrometry, Fluorescence
RN **9014-25-9 (RNA, Transfer)**
CN 0 (tRNA, phenylalanine-); 0 (Anticodon); 0 (Codon); 0 (**RNA**, Bacterial); 0 (**RNA**, Messenger); 0 (**RNA**, Transfer, Amino Acyl)

L134 ANSWER 93 OF 126 MEDLINE
AN 87254241 MEDLINE
DN 87254241
TI Models of nearly neutral mutations with particular implications for nonrandom usage of synonymous codons.
AU Li W H
SO JOURNAL OF MOLECULAR EVOLUTION, **(1987)** 24 (4) 337-45.
Journal code: J76. ISSN: 0022-2844.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198710
AB The population dynamics of nearly neutral mutations are studied using a single-site and a multisite model. In the latter model, the nucleotides in a sequence are completely linked and the selection schemes employed are additive, multiplicative, and additive with a threshold. Although the third selection scheme is very different from the first two, the three schemes produce identical results for a wide range of parameter values. Thus the present study provides a general theory for the population dynamics of nearly neutral mutations because the results can also be used to draw inferences about other selection schemes such as **stabilizing** selection and synergistic selection. It is shown that the number of slightly deleterious mutations accumulated in a sequence can be considerably larger under the multisite model than under the single-site model, particularly if the sequence is long or if the mutation rate per site is high. The results show that even a very slight selective difference between synonymous codons can produce a strong bias in codon usage. Three alternative explanations for the strong bias in codon usage in bacterial and yeast genes are considered. The implications of the present results for molecular evolution are discussed.
CT Check Tags: Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.
***Codon**
Evolution
*Models, Genetic
*Mutation
Probability
***RNA, Messenger**
Selection (Genetics)
CN 0 (Codon); 0 (**RNA**, Messenger)

L134 ANSWER 94 OF 126 MEDLINE
AN 87225671 MEDLINE
DN 87225671

TI Codon usage in streptococci.
AU Malke H
SO JOURNAL OF BASIC MICROBIOLOGY, **(1986)** 26 (10) 587-95.
Journal code: JOT. ISSN: 0233-111X.
CY GERMANY, EAST: German Democratic Republic
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198709
AB Codon usage was analysed for 14 streptococcal genes or significant open reading frames and found to be different from that in Escherichia coli and Bacillus subtilis. In particular, the preferred use of WWT codons over WWC was inconsistent with the rule of **optimal** codon-anticodon interaction energy. On the other hand, for SSTC codons, adherence to this rule was better in streptococci than in E. coli. A preliminary codon bias table generated with the Pustell computer program for the analysed streptococcal genes may prove useful for the detection of protein coding regions in newly sequenced DNAs from both streptococci and staphylococci.
CT Check Tags: Comparative Study
Bacillus subtilis: GE, genetics
***Codon**
Escherichia coli: GE, genetics
*Genes, Bacterial
***RNA, Messenger**
Species Specificity
*Streptococcus: GE, genetics
CN 0 (Codon); 0 (**RNA**, Messenger)

L134 ANSWER 95 OF 126 MEDLINE
AN 86286533 MEDLINE
DN 86286533
TI Codon usage in yeast: cluster analysis clearly differentiates highly and lowly expressed genes.
AU Sharp P M; Tuohy T M; Mosurski K R
SO NUCLEIC ACIDS RESEARCH, **(1986 Jul 11)** 14 (13) 5125-43.
Journal code: O8L. ISSN: 0305-1048.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198611
AB Codon usage data has been compiled for 110 yeast genes. Cluster analysis on relative synonymous codon usage revealed two distinct groups of genes. One group corresponds to highly expressed genes, and has much more extreme synonymous codon preference. The pattern of codon usage observed is consistent with that expected if a need to match abundant tRNAs, and intermediacy of tRNA-**mRNA** interaction energies are important selective constraints. Thus codon usage in the highly expressed group shows a higher correlation with tRNA abundance, a greater degree of third base pyrimidine bias, and a lesser tendency to the A+T richness which is characteristic of the yeast genome. The cluster analysis can be used to predict the likely level of gene expression of any gene, and identifies the pattern of codon usage likely to yield **optimal** gene expression in yeast.
CT Base Composition
***Codon**
Escherichia coli: GE, genetics
*Gene Expression Regulation
Histones: GE, genetics
Ribosomal Proteins: GE, genetics
***RNA, Messenger**
*Saccharomyces cerevisiae: GE, genetics
CN 0 (Codon); 0 (Histones); 0 (Ribosomal Proteins); 0 (**RNA**, Messenger)

L134 ANSWER 96 OF 126 MEDLINE

AN 86219708 MEDLINE
DN 86219708
TI Sequence verification of mutant codon assignments in trpA of Escherichia coli.
AU Tucker S D; Murgola E J
NC GM-21499 (NIGMS)
SO DNA, **(1986 Apr)** 5 (2) 123-8.
Journal code: EAW. ISSN: 0198-0238.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198609
AB Over the past 30 years, a variety of mutations have been characterized in trpA, the gene for the alpha-subunit of tryptophan synthetase in Escherichia coli. On the basis of amino acid sequence analyses, reversion studies, or suppressibility by codon-specific translational suppressors, base substitutions were deduced and codons assigned for each mutation. In the present study, three of the trpA mutants obtained over 25 years ago and a series of codon position 234 trpA mutants isolated more recently by specific selection methods have been cloned and characterized by DNA sequence analysis. Our results establish the reliability of the mutant codon assignments, confirm the validity of the selection and detection procedures used to obtain missense and nonsense mutations in trpA, and demonstrate that the trpA sequence has been **stably** maintained throughout 30 years of laboratory culturing and mutagenic treatments.
CT Check Tags: Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Amino Acid Sequence
*Bacterial Proteins: GE, genetics
Base Sequence
***Codon**
DNA, Bacterial: AN, analysis
Escherichia coli: GE, genetics
*Genes, Bacterial
Genes, Structural
Plasmids
***RNA, Messenger**
Suppression, Genetic
*Tryptophan Synthase: GE, genetics
CN EC 4.2.1.20 (Tryptophan Synthase); 0 (Bacterial Proteins); 0 (Codon); 0 (DNA, Bacterial); 0 (Plasmids); 0 (**RNA**, Messenger)

L134 ANSWER 97 OF 126 MEDLINE
AN 85270435 MEDLINE
DN 85270435
TI Molecular mechanism of codon recognition by tRNA species with modified uridine in the first position of the anticodon.
AU Yokoyama S; Watanabe T; Murao K; Ishikura H; Yamaizumi Z; Nishimura S; Miyazawa T
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, **(1985 Aug)** 82 (15) 4905-9.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198511
AB Proton NMR analyses have been made to elucidate the conformational characteristics of modified nucleotides as found in the first position of the anticodon of tRNA [derivatives of 5-methyl-2-thiouridine 5'-monophosphate (pxm5s2U) and derivatives of 5-hydroxyuridine 5'-monophosphate (pxo5U)]. In pxm5s2U, the C3'-endo form is extraordinarily more **stable** than the C2'-endo form for the ribose ring, because of the combined effects of the 2-thiocarbonyl group and the 5-substituent. By contrast, in pxo5U, the C2'-endo form is much more **stable** than the C3'-endo form, because of the interaction

between the 5-substituent and the 5'-phosphate group. The enthalpy differences between the C2'-endo form and the C3'-endo form have been obtained as 1.1, -0.7, and 0.1 kcal/mol (1 cal = 4.184 J) for pxm5s2U, pxo5U, and unmodified uridine 5'-monophosphate, respectively. These findings lead to the conclusion that xm5s2U in the first position of the anticodon exclusively takes the C3'-endo form to recognize adenosine (but not uridine) as the third letter of the codon, whereas xo5U takes the C2'-endo form as well as the C3'-endo form to recognize adenosine, guanosine, and uridine as the third letter of the codon on ribosome. Accordingly, the biological significance of such modifications of uridine to xm5s2U/xo5U is in the regulation of the conformational rigidity/flexibility in the first position of the anticodon so as to guarantee the correct and efficient translation of codons in protein biosynthesis.

CT Check Tags: Support, Non-U.S. Gov't
***Anticodon**
***Codon**
Hydrogen Bonding
Nuclear Magnetic Resonance
Nucleic Acid Conformation
***RNA, Messenger**
***RNA, Transfer**
***RNA, Transfer: GE, genetics**
Structure-Activity Relationship
*Uridine: AA, analogs & derivatives
Uridine: GE, genetics
RN 58-96-8 (Uridine); **9014-25-9 (RNA, Transfer)**
CN 0 (Anticodon); 0 (Codon); 0 (**RNA**, Messenger)

L134 ANSWER 98 OF 126 MEDLINE
AN 85237537 MEDLINE
DN 85237537
TI Codon equilibrium I: Testing for homogeneous equilibrium.
AU Wilbur W J
SO JOURNAL OF MOLECULAR EVOLUTION, **(1984-85)** 21 (2) 169-81.
Journal code: J76. ISSN: 0022-2844.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198510
AB We present theoretical considerations that suggest that synonymous-codon usage might be expected to be close to an equilibrium distribution given a very homogeneous process of silent substitution. By homogeneous we mean that substitution depends only on the two bases involved, so that 12 base-substitution rates completely describe the silent substitution process. We have developed a method of statistically testing for such homogeneous equilibrium and applied it to reported data on the codon usages of different classes of organisms. Weakly expressed bacterial sequences and both mammalian and nonmammalian eukaryotic sequences deviate significantly from a random pattern of codon usage, in the direction of homogeneous equilibrium. On the other hand, highly expressed bacterial sequences do not exhibit homogeneous equilibrium, which may be correlated with recent experimental results showing that they are **optimized** to accept the most abundant tRNAs. To examine the effect of amino acid replacements on the homogeneous model of silent substitution, we divided the amino acids with degenerate codes into two classes, those with high mutabilities and those with low, and performed the same analysis on bacterial and eukaryotic data sets. The codon sets of the highly mutable class of amino acids are not further from homogeneous equilibrium than are the codon sets of the class with low mutabilities. We also found for the eukaryotic data that these independent classes of codon sets show very similar equilibrium patterns. The various results suggest a high level of uniformity in the process of silent fixation in the different synonymous-codon sets, especially in eukaryotes.
CT Check Tags: Comparative Study

Amino Acid Sequence
Base Sequence
***Codon**
DNA: GE, genetics
Eukaryotic Cells: PH, physiology
*Evolution
*Genetic Code
Mutation
Probability
Prokaryotic Cells: PH, physiology
***RNA, Messenger**
RN 9007-49-2 (DNA)
CN 0 (Codon); 0 (**RNA**, Messenger)

L134 ANSWER 99 OF 126 MEDLINE
AN 85237493 MEDLINE
DN 85237493
TI Sense codons are found in specific contexts.
AU Yarus M; Folley L S
NC GM 30881 (NIGMS)
SO JOURNAL OF MOLECULAR BIOLOGY, **(1985 Apr 20)** 182 (4) 529-40.
Journal code: J6V. ISSN: 0022-2836.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198510
AB The sequence environment of codons in structural genes has been investigated statistically, using computer methods. A set of Escherichia coli genes with abundant products was compared with a set having low gene product levels, in order to detect potential differences associated with expression. The results show striking non-randomness in the nucleotides occurring near codons. These effects are, unexpectedly, very much larger and more homogeneous among the genes with rare products. The intensity of effects in weakly expressed genes suggests that such non-random sequence environments decrease expression. In the weakly expressed set of genes, the 5' neighbor of a codon, and all positions of the 3' neighbor codon are biased. In the highly expressed genes, the first nucleotide of the next codon is a uniquely affected site. The distribution of non-randomness in weakly expressed genes suggests that sequence bias is primarily due to a constraint acting directly on the secondary or tertiary structure of the codon/anticodon. In highly expressed genes, the observed bias suggests an interaction between the codon/anticodon and a site outside the codon/anticodon. Much of the tendency to non-random near-neighbor sequences in weakly expressed genes can be ascribed to a correlation between nearby nucleotides and the wobble nucleotide of the codon, despite the fact that selection of such correlations will alter the amino acid sequence. The favored pattern, in genes expressed at low level, is R YYR or Y RRY. R indicates purine, Y indicates pyrimidine; the space is the boundary between codons. It seems likely that this preference for nearby sequences is the physical basis of the genetic context effect. Under this assumption such sequence biases will affect expression. On this basis, we predict new sites for contextual mutations which decrease expression, and suggest strategy for the design of messages having **optimal** translational activity.
CT Check Tags: Support, U.S. Gov't, P.H.S.
Amino Acids: AN, analysis
Base Sequence
***Codon**
Computers
DNA, Bacterial
Escherichia coli: GE, genetics
Gene Expression Regulation
Genes, Bacterial
Genes, Structural
*Genetic Code

Probability
***RNA, Messenger**
CN 0 (Amino Acids); 0 (Codon); 0 (DNA, Bacterial); 0 (**RNA**, Messenger)

L134 ANSWER 100 OF 126 MEDLINE
AN 85170567 MEDLINE
DN 85170567
TI [Mechanism of the stereospecific **stabilization** of codon-anticodon complexes in ribosomes during translation]. Mekhanizm stereospetsificheskoi **stabilizatsii** kodon-antikodonnykh kompleksov na ribosomakh v khode transliatsii.
AU Potapov A P
SO ZHURNAL OBSHCHEI BIOLOGII, **(1985 Jan-Feb)** 46 (1) 63-77. Ref: 83
Journal code: YA8. ISSN: 0044-4596.
CY USSR
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA Russian
EM 198507
CT Check Tags: Animal
***Anticodon: ME, metabolism**
Binding Sites
***Codon: ME, metabolism**
Drug Interactions
English Abstract
Guanosine Triphosphate: ME, metabolism
Peptide Chain Elongation
Peptide Elongation Factors: ME, metabolism
Protein Binding
Protein Conformation
*Ribosomes: ME, metabolism
***RNA, Messenger: ME, metabolism**
***RNA, Transfer: ME, metabolism**
**RNA, Transfer, Amino Acyl: ME, metabolism**
Stereoisomerism
Temperature
*Translation, Genetic
RN 86-01-1 (Guanosine Triphosphate); **9014-25-9 (RNA, Transfer)**
CN 0 (tRNA, peptidyl-); 0 (Anticodon); 0 (Codon); 0 (Peptide Elongation Factors); 0 (**RNA**, Messenger); 0 (**RNA**, Transfer, Amino Acyl)

L134 ANSWER 101 OF 126 MEDLINE
AN 85131011 MEDLINE
DN 85131011
TI An alternative approach to deoxyoligonucleotides as hybridization probes by insertion of deoxyinosine at ambiguous codon positions.
AU Ohtsuka E; Matsuki S; Ikehara M; Takahashi Y; Matsubara K
SO JOURNAL OF BIOLOGICAL CHEMISTRY, **(1985 Mar 10)** 260 (5) 2605-8.
Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198506
AB Two deoxyoligonucleotide probes (23-mer and 26-mer) carrying deoxyinosine residues (I) at positions corresponding to ambiguous nucleotides derived from amino acid sequence have been synthesized by the phosphotriester method using a polymer support. The 23-mer and 26-mer corresponded to the **mRNA** for 8 amino acids from gastrin and 9 amino acids from cholecystokinin, respectively. The dIs have been used where the base in the third position of the amino acid codon is ambiguous. These deoxyoligonucleotides were used as probes for hybridization with colonies containing the corresponding cDNAs or genes. The hybrid formed between a gastrin clone and the 23-mer that harbors 5 dIs was dissociated at 50-55

degrees C, suggesting that deoxyinosine did not significantly effect the **stabilization** or destabilization of the DNA duplex. A similar result was obtained using the 26-mer that contains 5 dIs and a phage clone DNA of the cholecystokinin gene. Thus oligonucleotide probes with deoxyinosine residues at ambiguous points seem to be useful as hybridization probes for cloning genes for proteins containing amino acids with degenerate codons.

CT Check Tags: Support, Non-U.S. Gov't
Base Sequence
***Codon**
*Deoxyribonucleotides: CS, chemical synthesis
DNA: AN, analysis
Gastrins: GE, genetics
*Inosine: AA, analogs & derivatives
*Nucleic Acid Hybridization
***RNA, Messenger**
Temperature
Templates

RN 58-63-9 (Inosine); 890-38-0 (deoxyinosine); 9007-49-2 (DNA)

CN 0 (Codon); 0 (Deoxyribonucleotides); 0 (Gastrins); 0 (**RNA**, Messenger)

L134 ANSWER 102 OF 126 MEDLINE

AN 85073716 MEDLINE

DN 85073716

TI [Demonstration of a sudden change in the use of codons in the vicinity of transcription termination].
Mise en evidence d'une variation brusque de l'utilisation des codons au voisinage de la terminaison de la transcription.

AU Limaiem J; Henaut A

SO COMPTES RENDUS DE L ACADEMIE DES SCIENCES. SERIE III, SCIENCES DE LA VIE, **(1984)** 299 (8) 275-80.
Journal code: CA1. ISSN: 0764-4469.

CY France

DT Journal; Article; (JOURNAL ARTICLE)

LA French

FS Priority Journals

EM 198504

AB A characteristic profile of fluctuations in the use of codons is seen in bacteriophages, Mammal mitochondria and animal viruses. Following DNA in the direction of transcription, one goes slowly from an area rich in codons ending by C to an area rich in codons ending by T and then one falls abruptly in an area rich in C. The termination of transcription is located in the area where the use of codons changes suddenly. It seems that the choice of codons ending by T or C is directed by the necessity to have a variation in the **stability** of the DNA. We propose a dynamic model where large scale variations of the **stability** of the DNA regulates the speed of propagation of the **RNA** -polymerase.

CT Check Tags: Animal
***Codon: ME, metabolism**
***DNA-Directed RNA Polymerase: ME, metabolism**
English Abstract
Models, Genetic
***RNA, Messenger: ME, metabolism**
*Transcription, Genetic

CN EC 2.7.7.6 (DNA-Directed **RNA** Polymerase); 0 (Codon); 0 (**RNA**, Messenger)

L134 ANSWER 103 OF 126 MEDLINE

AN 85051366 MEDLINE

DN 85051366

TI Yeast tRNAAsp: codon and wobble codon-anticodon interactions. A transferred nuclear Overhauser enhancement study.

AU Gronenborn A M; Clore G M; McLaughlin L W; Graeser E; Lorber B; Giege R

SO EUROPEAN JOURNAL OF BIOCHEMISTRY, **(1984 Dec 3)** 145 (2) 359-64.

Journal code: EMZ. ISSN: 0014-2956.
CY GERMANY, WEST: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198503
AB The conformations of the ribotrinucleoside bisphosphates GpApC and GpApU, the codon and wobble codon for aspartic acid respectively, bound to yeast tRNAAsp in solution, have been examined by means of time-dependent transferred nuclear Overhauser enhancement measurements to determine distances between bound ligand protons. The conformations of the two bound ribotrinucleoside bisphosphates are shown to be very similar with an overall root-mean-square difference in interproton distances of 0.03 nm. The ribose conformations of all the residues are 3'-endo; the glycosidic bond torsion angles of the A and C residues of GpApC and of the A and U residues of GpApU are in the low anti range. These features are typical of an A-**RNA** type structure. In contrast, the G residue of both GpApC and GpApU exists as a mixture of syn and anti conformations. The overall conformation of the two bound ribotrinucleoside bisphosphates is also similar to A-**RNA** and the **stability** of the complexes is enhanced by extensive base-base stacking interactions. In addition, it is shown that the binding of the codon GpApC to tRNAAsp induces self-association into a multicomplex system consisting of four GpApC-tRNAAsp complexes, whereas the wobble codon GpApU fails to induce any observable self-association.
CT Check Tags: Support, Non-U.S. Gov't
***Anticodon**
Aspartic Acid
***Codon**
Hydrogen Bonding
Nuclear Magnetic Resonance
Nucleic Acid Conformation
***RNA, Messenger**
***RNA, Transfer**
Saccharomyces cerevisiae: GE, genetics
RN 56-84-8 (Aspartic Acid); **9014-25-9 (RNA, Transfer)**
CN 0 (Anticodon); 0 (Codon); 0 (**RNA**, Messenger)

L134 ANSWER 104 OF 126 MEDLINE
AN 84307562 MEDLINE
DN 84307562
TI Protein synthesis in rabbit reticulocytes: requirements for Met-tRNAf . 40S preinitiation complex formation with AUG-codon and physiological **mRNAs**.
AU Roy R; Nasrin N; Ahmad M F; Gupta N K
NC GM 22079 (NIGMS)
SO BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, **(1984 Aug 16)** 122 (3) 1418-25.
Journal code: 9Y8. ISSN: 0006-291X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198412
AB Under standard conditions, in the presence of GTP, highly purified eIF-2 and Co-eIF-2 factor preparations efficiently stimulated AUG-codon dependent but not physiological **mRNA**-dependent Met-tRNAf binding to 40S ribosomes. Replacement of GTP by a nonhydrolyzable GTP analog, GMP-PNP, in the above system, gave significant stimulation of Met-tRNAf binding to 40S ribosomes dependent on physiological **mRNAs**. Lower but significant stimulation of Met-tRNAf binding to 40S ribosomes was also observed when GTP was used in the presence of nucleoside 5'-diphosphate kinase (NDK) and ATP. ATP alone in the absence of NDK had no significant effect. This is the first report on the formation of a **stable** Met-tRNAf . 40S initiation complex dependent on physiological **mRNAs** and the factor requirements for such complex formation.

CT Check Tags: Animal; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
*Blood Proteins
***Codon: GE, genetics**
Globin: GE, genetics
Guanosine Triphosphate: PD, pharmacology
Guanylyl Imidodiphosphate: PD, pharmacology
Kinetics
*Peptide Initiation Factors: BL, blood
Rabbits
*Reticulocytes: ME, metabolism
***RNA, Messenger: GE, genetics**
**RNA, Transfer, Amino Acyl: BL, blood**
*Translation, Genetic
Translation, Genetic: DE, drug effects
RN 34273-04-6 (Guanylyl Imidodiphosphate); 86-01-1 (Guanosine Triphosphate); 9004-22-2 (Globin)
CN 0 (eIF-2); 0 (tRNA, formylmethionine-); 0 (Blood Proteins); 0 (Codon); 0 (Guanine Nucleotide Exchange Factors); 0 (Peptide Initiation Factors); 0 (**RNA**, Messenger); 0 (**RNA**, Transfer, Amino Acyl)

L134 ANSWER 105 OF 126 MEDLINE
AN 84188487 MEDLINE
DN 84188487
TI Structure of the ribotrinucleoside diphosphate codon UpUpC bound to tRNAPhe from yeast. A time-dependent transferred nuclear Overhauser enhancement study.
AU Clore G M; Gronenborn A M; McLaughlin L W
SO JOURNAL OF MOLECULAR BIOLOGY, **(1984 Mar 25)** 174 (1) 163-73.
Journal code: J6V. ISSN: 0022-2836.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198408
AB The structure of the ribotrinucleoside diphosphate UpUpC, the codon for phenylalanine, bound to yeast tRNAPhe in solution is elucidated using time-dependent proton-proton transferred nuclear Overhauser enhancement measurements to determine distances between bound ligand protons. The glycosidic bond and ribose conformations are low anti and 3'-endo, respectively, typical of an A-**RNA** type structure. The main chain torsion angles are all within the range of those expected for A-**RNA** but small differences from those in conventional A-**RNA** 11 result in a special structure with a larger rotation per residue (40 to 45 degrees compared to 32.7 degrees in R-**RNA** 11) and almost perfect stacking of the bases. These two structural features, which are similar to those found in the anticodon triplet of the monoclinic crystal form of tRNAPhe, can account for the known greater **stability** of the codon-anticodon complex relative to an equivalent double helical **RNA** trimer with a conventional A-**RNA** structure.
CT Check Tags: Support, Non-U.S. Gov't
***Codon**
*Cytidine: AA, analogs & derivatives
Cytidine: GE, genetics
Macromolecular Systems
Models, Genetic
Nuclear Magnetic Resonance
Nucleic Acid Conformation
*Oligonucleotides: GE, genetics
*Oligoribonucleotides: GE, genetics
***RNA, Messenger**
***RNA, Transfer, Amino Acyl: GE, genetics**
*Saccharomyces cerevisiae: GE, genetics
Time Factors
RN 2791-46-0 (5'-r(uridylyl-uridylyl cytidine)); 65-46-3 (Cytidine)
CN 0 (tRNA, phenylalanine-); 0 (Codon); 0 (Macromolecular Systems); 0 (Oligonucleotides); 0 (Oligoribonucleotides); 0 (**RNA**,

Messenger); 0 (**RNA**, Transfer, Amino Acyl)

L134 ANSWER 106 OF 126 MEDLINE
AN 84135791 MEDLINE
DN 84135791
TI High guanine plus cytosine content in the third letter of codons of an extreme thermophile. DNA sequence of the isopropylmalate dehydrogenase of Thermus thermophilus.
AU Kagawa Y; Nojima H; Nukiwa N; Ishizuka M; Nakajima T; Yasuhara T; Tanaka T; Oshima T
SO JOURNAL OF BIOLOGICAL CHEMISTRY, **(1984 Mar 10)** 259 (5) 2956-60.
Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-K01444
EM 198406
AB In studies on the cause of the extreme **stability** of the macromolecules of Thermus thermophilus HB8, the leuB gene coding for 3-isopropylmalate dehydrogenase of the leucine synthesis pathway and its flanking regions were cloned and sequenced. The leuB gene of T. thermophilus was expressed in a leuB-less mutant of Escherichia coli, and thermostable dehydrogenase was purified from an extract of the cells. The primary structure of the thermophilic isopropylmalate dehydrogenase was deduced from the nucleotide sequence leuB gene (1017 base pairs) and the amino acid sequence of the peptides isolated from the purified dehydrogenase. The thermophilic dehydrogenase has Mr = 35,968, and the value was close to that determined for the monomer of dehydrogenase (36,000) by gel electrophoresis. The molecular weight of active dimeric dehydrogenase was found to be 73,000 by high speed liquid chromatography. The primary structure of dehydrogenase was consistent with the amino acid composition of the dehydrogenase. In contrast to the isopropylmalate dehydrogenase of E. coli which contains 8 cysteine residues, there was no cysteine in thermophilic isopropylmalate dehydrogenase. The 5'-noncoding region contained a typical Shine-Dalgarno sequence. The guanine plus cytosine content of the coding region was 70.1%, and that of the third letter of the codons was extremely high (89.4%).
CT Check Tags: Support, Non-U.S. Gov't
*Alcohol Oxidoreductases: GE, genetics
Amino Acid Sequence
Base Composition
Base Sequence
***Codon: GE, genetics**
*Cytosine: AN, analysis
DNA Restriction Enzymes
*DNA, Bacterial: GE, genetics
*Genes, Bacterial
*Genes, Structural
*Guanine: AN, analysis
***RNA, Messenger: GE, genetics**
Thermus: EN, enzymology
*Thermus: GE, genetics
RN 71-30-7 (Cytosine); 73-40-5 (Guanine)
CN EC 1.1 (Alcohol Oxidoreductases); EC 1.1.1.85 (3-isopropylmalate dehydrogenase); EC 3.1.21 (DNA Restriction Enzymes); 0 (Codon); 0 (DNA, Bacterial); 0 (**RNA**, Messenger)

L134 ANSWER 107 OF 126 MEDLINE
AN 84032548 MEDLINE
DN 84032548
TI Unconventional reading of the glycine codons.
AU Samuelsson T; Axberg T; Boren T; Lagerkvist U
SO JOURNAL OF BIOLOGICAL CHEMISTRY, **(1983 Nov 10)** 258 (21) 13178-84.
Journal code: HIV. ISSN: 0021-9258.

CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198402
AB We have used a protein-synthesizing in vitro system programmed with the phage message MS2-**RNA** to investigate the ability of glycyl-tRNAs with different anticodons to read the glycine codons. Under conditions of no competition, when the glycyl-tRNA analyzed was the only source of glycine for protein synthesis, each of the isoacceptors tested, tRNA1Gly (anticodon CCC), tRNA2Gly (anticodon N/UCC), tRNA3Gly (anticodon GCC) from Escherichia coli, and tRNAGly (anticodon UCC) from Mycoplasma mycoides, could read all of the glycine codons in the MS2 coat protein cistron (GGU, GGC, GGA, and GGG). However, tRNA1Gly seemed to have difficulties reading through the whole cistron. Experiments in which two glycyl-tRNAs competed for the same codon showed that the mycoplasma tRNAGly (anticodon UCC) was almost as efficient in the unorthodox reading of the codons GGU and GGC as it was in conventional reading. It would seem to be the only tRNAGly present in Mycoplasma mycoides and our results are consistent with this finding since the mycoplasma tRNAGly appears to have been designed to read all four glycine codons with approximately equal efficiency. The competition experiments furthermore showed that E. coli tRNA1Gly (anticodon CCC) reads the codon GGA more efficiently than it reads GGU and GGC suggesting that the mispair C . A between the wobble position of the anticodon and the third codon position might have appreciable **stability**.
CT Check Tags: Comparative Study; Support, Non-U.S. Gov't
Amino Acid Sequence
Base Sequence
***Codon: GE, genetics**
*Coliphages: GE, genetics
*Escherichia coli: GE, genetics
*Glycine: GE, genetics
*Mycoplasma mycoides: GE, genetics
***RNA, Messenger: GE, genetics**
***RNA, Transfer, Amino Acyl: GE, genetics**
**RNA, Viral: GE, genetics**
Species Specificity
RN 56-40-6 (Glycine)
CN 0 (tRNA, glycine-); 0 (Codon); 0 (**RNA**, Messenger); 0 (**RNA**, Transfer, Amino Acyl); 0 (**RNA**, Viral)

L134 ANSWER 108 OF 126 MEDLINE
AN 83210229 MEDLINE
DN 83210229
TI Effect of codon shortening and the antibiotics viomycin and sparsomycin upon the behaviour of bound aminoacyl-tRNA. Decoding at the ribosomal A site.
AU Hornig H; Woolley P; Luhrmann R
SO FEBS LETTERS, **(1983 Jun 13)** 156 (2) 311-5.
Journal code: EUH. ISSN: 0014-5793.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198309
AB 70 S ribosomes were programmed with initiator tRNA and messenger oligonucleotides AUG(U)n and AUG(C)n, where n = 1, 2 or 3. The binding of the ternary complexes [Phe-tRNA X EF-Tu X GTP] and [Pro-tRNA X EF-Tu X GTP] to the programmed ribosomes was studied. If codon-anticodon interaction is restricted to only one basepair, the ternary complex leaves the ribosome before GTP hydrolysis. Two basepairs allow hydrolysis of GTP, but the aminoacyl-tRNA dissociates and is recycled, resulting in wastage of GTP. Three basepairs result in apparently **stable** binding of aminoacyl-tRNA to the ribosome. The antibiotic sparsomycin weakens the binding by an amount roughly equivalent to one messenger base, while

viomycin has the reverse effect.
CT *Antibiotics, Antineoplastic: PD, pharmacology
Binding Sites: DE, drug effects
Chemistry
***Codon: ME, metabolism**
*Genetic Code: DE, drug effects
Guanosine Triphosphate: ME, metabolism
Hydrolysis
*Ribosomes: ME, metabolism
***RNA, Messenger: ME, metabolism**
***RNA, Transfer, Amino Acyl: ME, metabolism**
*Sparsomycin: PD, pharmacology
*Viomycin: PD, pharmacology
RN 1404-64-4 (Sparsomycin); 32988-50-4 (Viomycin); 86-01-1 (Guanosine Triphosphate)
CN 0 (Codon); 0 (**RNA**, Messenger); 0 (**RNA**, Transfer, Amino Acyl)

L134 ANSWER 109 OF 126 MEDLINE
AN 83049081 MEDLINE
DN 83049081
TI Codon:anticodon and anticodon:anticodon interaction: evaluation of equilibrium and kinetic parameters of complexes involving a g:u wobble.
AU Labuda D; Grosjean H; Striker G; Porschke D
SO BIOCHIMICA ET BIOPHYSICA ACTA, **(1982 Sep 27)** 698 (3) 230-6.
Journal code: A0W. ISSN: 0006-3002.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198303
AB In order to learn about the effect of the G:U wobble interaction we characterized to codon:anticodon binding between triplets: UUC, UUU and yeast tRNAPhe (anticodon GmAA) as well as the anticodon:anticodon binding between Escherichia coli tRNAGlu2, E. coli tRNALys (anticodons: mam5s2UUC, and mam5S2UUU, respectively) and tRNAPhe from yeast and E. coli (anticodon GAA) using equilibrium fluorescence titrations and temperature jump measurements with fluorescence and absorption detection. The difference in **stability** constants between complexes involving a G:U pair rather than a usual G:C basepair is in the range of one order magnitude and is mainly due to the shorter lifetime of the complex involving G:U in the wobble position. This difference is more pronounced when the codon triplet is structured, i.e., is built in the anticodon loop of a tRNA. The reaction enthalpies of the anticodon:anticodon complexes involving G:U mismatching were found to be about 4 kcal/mol smaller, and the melting temperatures more than 20 degrees C lower, than those of the corresponding complexes with the G:C basepair. The results are discussed in terms of different strategies that might be used in the cell in order to minimize the effect of different lifetimes of codon-tRNA complexes. Differences in these lifetimes may be used for the modulation of the translation efficiency.
CT Check Tags: Support, Non-U.S. Gov't
***Anticodon: ME, metabolism**
Binding, Competitive
***Codon: ME, metabolism**
Escherichia coli: GE, genetics
Kinetics
***RNA, Messenger: ME, metabolism**
***RNA, Transfer: ME, metabolism**
Translation, Genetic
RN **9014-25-9 (RNA, Transfer)**
CN 0 (Anticodon); 0 (Codon); 0 (**RNA**, Messenger)

L134 ANSWER 110 OF 126 MEDLINE
AN 83028535 MEDLINE
DN 83028535

TI Preferential codon usage in prokaryotic genes: the **optimal** codon-anticodon interaction energy and the selective codon usage in efficiently expressed genes.
AU Grosjean H; Fiers W
SO GENE, **(1982 Jun)** 18 (3) 199-209. Ref: 72
Journal code: FOP. ISSN: 0378-1119.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 198302
AB By considering the nucleotide sequence of several highly expressed coding regions in bacteriophage MS2 and **mRNAs** from Escherichia coli, it is possible to deduce some rules which govern the selection of the most appropriate synonymous codons NNU or NNC read by tRNAs having GNN, QNN or INN as anticodon. The rules fit with the general hypothesis that an efficient in-phase translation is facilitated by proper choice of degenerate codewords promoting a codon-anticodon interaction with intermediate strength (**optimal** energy) over those with very strong or very weak interaction energy. Moreover, codons corresponding to minor tRNAs are clearly avoided in these efficiently expressed genes. These correlations are clearcut in the normal reading frame but not in the corresponding frameshift sequences +1 and +2. We hypothesize that both the **optimization** of codon-anticodon interaction energy and the adaptation of the population to codon frequency or vice versa in highly expressed **mRNAs** of E. coli are part of a strategy that **optimizes** the efficiency of translation. Conversely, codon usage in weakly expressed genes such as repressor genes follows exactly the opposite rules. It may be concluded that, in addition to the need for coding an amino acid sequence, the energetic consideration for codon-anticodon pairing, as well as the adaptation of codons to the tRNA population, may have been important evolutionary constraints on the selection of the **optimal** nucleotide sequence.
CT Check Tags: Support, Non-U.S. Gov't
***Anticodon: GE, genetics**
Base Sequence
***Codon: GE, genetics**
*Coliphages: GE, genetics
*Escherichia coli: GE, genetics
*Genes, Bacterial
*Genes, Viral
***RNA, Messenger: GE, genetics**
***RNA, Transfer: GE, genetics**
***RNA, Viral: GE, genetics**
Transcription, Genetic
Translation, Genetic
Viral Proteins: GE, genetics
RN **9014-25-9 (RNA, Transfer)**
CN 0 (Anticodon); 0 (Codon); 0 (**RNA**, Messenger); 0 (**RNA**, Viral); 0 (Viral Proteins)

L134 ANSWER 111 OF 126 MEDLINE
AN 83023172 MEDLINE
DN 83023172
TI **RNA** folding is unaffected by the nonrandom degenerate codon choice.
AU Nussinov R
SO BIOCHIMICA ET BIOPHYSICA ACTA, **(1982 Aug 30)** 698 (2) 111-5.
Journal code: A0W. ISSN: 0006-3002.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198302
AB The frequent suggestion that the nonrandom codon usage is explained by its

forming more **stable mRNAs** is tested in 22 genes. Only the histones, globins, and the rat preproinsulin gene show a correlation between the preferred degenerate codons and the **stability** of the secondary structure of the their **mRNAs**. However, the examined members from the histone and globin gene families, both among the oldest, in evolutionary sense, eukaryotic genes, have a high GC content (approx. 56% compared to an average of 42% in all eukaryotes) which is reflected in their degenerate codon choice and thus in their more **stable** folding.

CT Check Tags: Animal
***Codon: GE, genetics**
*Genes, Structural
Globin: GE, genetics
Histones: GE, genetics
*Nucleic Acid Conformation
Proteins: GE, genetics
Rabbits
Rats
***RNA, Messenger: GE, genetics**
Thermodynamics
RN 9004-22-2 (Globin)
CN 0 (Codon); 0 (Histones); 0 (**RNA**, Messenger)

L134 ANSWER 112 OF 126 MEDLINE
AN 82170439 MEDLINE
DN 82170439
TI Correlation between the abundance of Escherichia coli transfer **RNAs** and the occurrence of the respective codons in its protein genes: a proposal for a synonymous codon choice that is **optimal** for the E. coli translational system.
AU Ikemura T
SO JOURNAL OF MOLECULAR BIOLOGY, **(1981 Sep 25)** 151 (3) 389-409.
Journal code: J6V. ISSN: 0022-2836.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198208
CT Check Tags: Support, Non-U.S. Gov't
***Codon**
*Escherichia coli: GE, genetics
Evolution
*Genes, Structural
Models, Genetic
***RNA, Bacterial**
**RNA, Bacterial: AN, analysis**
***RNA, Messenger**
***RNA, Transfer**
**RNA, Transfer: AN, analysis**
*Translation, Genetic
RN **9014-25-9 (RNA, Transfer)**
CN 0 (Codon); 0 (**RNA**, Bacterial); 0 (**RNA**, Messenger)

L134 ANSWER 113 OF 126 MEDLINE
AN 82150194 MEDLINE
DN 82150194
TI Key for protein coding sequences identification: computer analysis of codon strategy.
AU Rodier F; Gabarro-Arpa J; Ehrlich R; Reiss C
SO NUCLEIC ACIDS RESEARCH, **(1982 Jan 11)** 10 (1) 391-402.
Journal code: O8L. ISSN: 0301-5610.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198207

AB The signal qualifying an AUG or GUG as an initiator in **mRNAs** processed by E. coli ribosomes is not found to be a systematic, literal homology sequence. In contrast, **stability** analysis reveals that initiators always occur within nucleic acid domains of low **stability**, for which a high A/U content is observed. Since no aminoacid selection pressure can be detected at N-termini of the proteins, the A/U enrichment results from a biased usage of the code degeneracy. A computer analysis is presented which allows easy detection of the codon strategy. N-terminal codons carry rather systematically A or U in third position, which suggests a mechanism for translation initiation and helps to detect protein coding sequences in sequenced DNA.

CT *Amino Acid Sequence
*Bacterial Proteins: GE, genetics
*Base Sequence
***Codon: GE, genetics**
Coliphages: GE, genetics
*Computers
*DNA, Bacterial: GE, genetics
Escherichia coli: ME, metabolism
Genes, Structural
Methods
Ribosomes: ME, metabolism
***RNA, Messenger: GE, genetics**
Translation, Genetic

CN 0 (Bacterial Proteins); 0 (Codon); 0 (DNA, Bacterial); 0 (**RNA**, Messenger)

L134 ANSWER 114 OF 126 MEDLINE
AN 82060328 MEDLINE
DN 82060328
TI Possibility of extensive neutral evolution under **stabilizing** selection with special reference to nonrandom usage of synonymous codons.
AU Kimura M
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, **(1981 Sep)** 78 (9) 5773-7.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198203

AB The rate of evolution in terms of the number of mutant substitutions in a finite population is investigated assuming a quantitative character subject to **stabilizing** selection, which is known to be the most prevalent type of natural selection. It is shown that, if a large number of segregating loci (or sites) are involved, the average selection coefficient per mutant under **stabilizing** selection may be exceedingly small. These mutants are very slightly deleterious but nearly neutral, so that mutant substitutions are mainly controlled by random drift, although the rate of evolution may be lower as compared with the situation in which all the mutations are strictly neutral. This is treated quantitatively by using the diffusion equation method in population genetics. A model of random drift under **stabilizing** selection is then applied to the problem of "nonrandom" or unequal usage of synonymous codons, and it is shown that such nonrandomness can readily be understood within the framework of the neutral mutation--random drift hypothesis (the neutral theory, for short) of molecular evolution.

CT Check Tags: Support, Non-U.S. Gov't
Alleles
***Codon**
*Evolution
Gene Frequency
Mutation
Phenotype
Probability
***RNA, Messenger**

Selection (Genetics)
CN 0 (Codon); 0 (**RNA**, Messenger)

L134 ANSWER 115 OF 126 MEDLINE
AN 81236553 MEDLINE
DN 81236553
TI Effect of threonylcarbamoyl modification (t6A) in yeast tRNA Arg III on codon-anticodon and anticodon-anticodon interactions. A thermodynamic and kinetic evaluation.
AU Weissenbach J; Grosjean H
SO EUROPEAN JOURNAL OF BIOCHEMISTRY, **(1981 May)** 116 (1) 207-13.
Journal code: EMZ. ISSN: 0014-2956.
CY GERMANY, WEST: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198111
AB The effect of N-[9-(beta-D-ribofuranosyl) purin-6-ylcarbamoyl]threonine (t6A) adjacent to anticodon U-C-U of yeast tRNA Arg III (where U is a modified U), compared to its unmodified adenosine counterpart, has been evaluated by three independent methods: (a) the polynucleotide-directed binding of tRNA on ribosomes, (b) the ribosome-free trinucleotide binding to the anticodon, (c) the anticodon-anticodon binding test. The results obtained by these three methods indicate a small but significant **stabilization** effect of t6A on the binding of yeast tRNA Arg III with (a) poly(A,G) in the presence of Escherichia coli ribosomes, (b) free A-G-A triplet, and (c) E. coli tRNA Ser V (anticodon G-G-A). We therefore conclude that the **stabilization** effect of t6A occurs on U x A and U x G base pairs adjacent to the 5' side of the modified nucleoside, most probably by stacking.
CT Check Tags: Support, Non-U.S. Gov't
Adenosine: AA, analogs & derivatives
***Anticodon: ME, metabolism**
Base Composition
***Codon: ME, metabolism**
*Escherichia coli: ME, metabolism
Kinetics
*Purine Nucleosides: ME, metabolism
Ribosomes: ME, metabolism
***RNA, Messenger: ME, metabolism**
***RNA, Transfer: ME, metabolism**
***RNA, Transfer, Amino Acyl: ME, metabolism**
Saccharomyces cerevisiae: GE, genetics
Thermodynamics
*Threonine: AA, analogs & derivatives
Threonine: ME, metabolism
RN 24719-82-2 (N(6)-(N-threonylcarbonyl)adenosine); 58-61-7 (Adenosine); 72-19-5 (Threonine); **9014-25-9 (RNA, Transfer)**
CN 0 (tRNA, arginine-); 0 (Anticodon); 0 (Codon); 0 (Purine Nucleosides); 0 (**RNA**, Messenger); 0 (**RNA**, Transfer, Amino Acyl)

L134 ANSWER 116 OF 126 MEDLINE
AN 81184709 MEDLINE
DN 81184709
TI Does quantitative tRNA adaptation to codon content in **mRNA** **optimize** the ribosomal translation efficiency? Proposal for a translation system model.
AU Chavancy G; Garel J P
SO BIOCHIMIE, **(1981 Mar)** 63 (3) 187-95.
Journal code: A14. ISSN: 0300-9084.
CY France
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198109
AB Neither a dynamic nor an energetic approach of the translation process has

taken into account that intracellular levels of iso-tRNA species are adapted or adjusted to the codon frequency of **mRNA** being decoded (Bombyx mori silk gland, rabbit reticulocyte). A critical study of available experimental data suggests that the average elongation rate of a protein is maximized in the presence of an adapted tRNA population, usually an homologous tRNA. In addition, the amount of synthesized protein parallels that of corresponding **mRNA**. Other evidences--including in vitro and in vivo elongation assays with fibroin **mRNA**--show that individual elongation rates are not uniform. Pauses occur at certain sites of the **mRNA** chain. The relative lifetime of these pauses depends on the tRNA pool used. Finally, it appears that translation accuracy also depends on the balanced tRNA population. We propose to explain these different effects by using a codon-anticodon recognition model, called "trial and error system" based on a stochastic processing of the ribosome. Accordingly, various acylated tRNA species which surround a ribosome randomly encounter the receptor A site. Every trapped tRNA species is tested for a proper pairing with the codon to be recognized at the level of a comparator or discriminator function. If the pairing is correct, transpeptidation becomes irreversible. If not, the aminoacyl-tRNA is rejected and another randomly trapped tRNA is processed in turn. Mathematical analysis of this model shows that the mean number of trials used for translating the whole sequence of a **mRNA** is minimized when the proportion of different iso-tRNA species is correlated with the square root of codon frequency. Quantitations of reticulocyte tRNA support such a parabolic relation. Our translation system model brings some light into the role of tRNA adaptation for **optimizing** translation efficiency, i.e. maximizing both speed and accuracy. Some consequences of the model are discussed.

CT Check Tags: Support, Non-U.S. Gov't
**Codon: AN, analysis**
***Codon: GE, genetics**
Kinetics
Models, Genetic
Peptide Chain Elongation
***RNA, Messenger: GE, genetics**
***RNA, Transfer: AN, analysis**
*Translation, Genetic

RN **9014-25-9 (RNA, Transfer)**

CN 0 (Codon); 0 (**RNA**, Messenger)

L134 ANSWER 117 OF 126 MEDLINE

AN 81124301 MEDLINE

DN 81124301

TI Dinucleotide codon-anticodon interaction as a minimum requirement for ribosomal aa-tRNA binding: **stabilisation** by viomycin of aa-tRNA in the A site.

AU Luhrmann R

SO NUCLEIC ACIDS RESEARCH, **(1980 Dec 11)** 8 (23) 5813-24.
Journal code: O8L. ISSN: 0301-5610.

CY ENGLAND: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 198106

AB The requirements for the decoding process at the ribosomal A site have been investigated in the presence of viomycin. For these studies natural **mRNA** was replaced either by the synthetic oligonucleotide A-U-G(-U)n, with 0 less than or equal to n less than or equal to 4, or by a physical mixture of the oligonucleotides A-U-G and various oligo(U) sequences. Thus the effect of the "removal" of selected covalent bonds from the sequence A-U-G(U)n could be studied. When the ribosomal P site contains tRNAMetf, then normally the full hexanucleotide "messenger" A-U-G-U-U-U is needed for the EF-Tu-mediated binding of Phe-tRNA into the A site. However in presence of viomycin the pentanucleotide A-U-G-U-U suffices for this. It is also possible in the presence of viomycin to replace A-U-G-U and U-U. In all the above systems the binding of Phe-tRNA

required the presence of EF-Tu and GTP. The results suggest that viomycin reinforces interactions between aa-tRNA and the A site after the codon-anticodon recognition step.
CT Check Tags: Comparative Study; Support, Non-U.S. Gov't
***Anticodon: ME, metabolism**
Binding Sites
***Codon: ME, metabolism**
Dipeptides: BI, biosynthesis
Escherichia coli: ME, metabolism
Oligoribonucleotides: ME, metabolism
Ribosomes: DE, drug effects
*Ribosomes: ME, metabolism
**RNA, Bacterial: ME, metabolism**
***RNA, Messenger: ME, metabolism**
***RNA, Transfer: ME, metabolism**
***RNA, Transfer, Amino Acyl: ME, metabolism**
*Viomycin: PD, pharmacology
RN 32988-50-4 (Viomycin); **9014-25-9 (RNA, Transfer)**
CN 0 (Anticodon); 0 (Codon); 0 (Dipeptides); 0 (Oligoribonucleotides); 0 ( **RNA**, Bacterial); 0 (**RNA**, Messenger); 0 (**RNA**, Transfer, Amino Acyl)

L134 ANSWER 118 OF 126 MEDLINE
AN 81093990 MEDLINE
DN 81093990
TI A GTPase reaction accompanying the rejection of Leu-tRNA2 by UUU-programmed ribosomes. Proofreading of the codon-anticodon interaction by ribosomes.
AU Thompson R C; Dix D B; Gerson R B; Karim A M
NC GM 24983 (NIGMS)
SO JOURNAL OF BIOLOGICAL CHEMISTRY, **(1981 Jan 10)** 256 (1) 81-6. Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198105
AB The characteristics of a GTPase reaction between poly(U)-programmed ribosomes, EFTu . GTP, and the near-cognate aminoacyl (aa)-tRNA, Leu-tRNA Leu 2, have been studied to assess the role of this reaction in proofreading of the codon-anticodon interaction. The reaction resembles the GTPase reaction with cognate aa-tRNAs and EFTu . GTP in its substrate requirements, in its involving EFTu . GTP . aa-tRNA ternary complexes, and in its requiring a free ribosomal A-site. The noncognate reaction differs from the cognate one in that aa-tRNA becomes **stably** bound to the ribosomes only 5% of the time; it therefore seems best characterized as an abortive enzymatic binding reaction. The rate of reaction is a significant fraction (4%) of that of the cognate aa-tRNA, indicating that recognition of ternary complexes by ribosomes involves a level of error greater than that of translation as a whole. The rejection of the noncognate aa-tRNA following GTP hydrolysis is therefore a vital step in the translation process and fulfills the criteria set for a proofreading reaction. Leu-tRNA Leu 2 which escapes rejection through proofreading, forms a **stable** complex with the ribosomal A-site, so it appears that the Leu-tRNA2 which was rejected never reached the A-site and that proofreading precedes full A-site binding.
CT Check Tags: Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
***Anticodon: ME, metabolism**
***Codon: ME, metabolism**
*Escherichia coli: ME, metabolism
*GTP Phosphohydrolases: ME, metabolism
Kinetics
*Phosphoric Monoester Hydrolases: ME, metabolism
*Poly U: ME, metabolism
Polyribosomes: ME, metabolism
*Ribosomes: ME, metabolism

***RNA, Messenger: ME, metabolism**
***RNA, Transfer: ME, metabolism**
***RNA, Transfer, Amino Acyl: ME, metabolism**
RN 27416-86-0 (Poly U); 73562-14-8 (tRNA, leucine-); **9014-25-9 (RNA, Transfer)**
CN EC 3.1.3 (Phosphoric Monoester Hydrolases); EC 3.6.1.- (GTP Phosphohydrolases); 0 (Anticodon); 0 (Codon); 0 (**RNA**, Messenger); 0 (**RNA**, Transfer, Amino Acyl)

L134 ANSWER 119 OF 126 MEDLINE
AN 81042559 MEDLINE
DN 81042559
TI [Use of the degeneracy of the genetic code by selective pressure to cut up genes of procaryote genomes].
Utilisation de la degenerescence du code genetique par la pression de selection pour le decoupage en g`enes du genome des procaryotes.
AU Rodier F; Gabarro-Arpa J; Ehrlich R; Reiss C
SO COMPTES RENDUS DES SEANCES DE L ACADEMIE DES SCIENCES. SERIE D, SCIENCES NATURELLES, **(1980 Sep 15)** 291 (2) 199-202.
Journal code: C9E. ISSN: 0567-655X.
CY France
DT Journal; Article; (JOURNAL ARTICLE)
LA French
FS Priority Journals
EM 198103
AB The DNA sequences of three bacteriophages are analysed in order to localise those parts coding for a protein. A weak **stability** on the DNA molecule allows us to characterize the beginning and the end of genes. A survey of the codons used shows that the cause for this weak **stability** is the systematic use of A-T bases in third position, which is made possible by the degeneracy of the genetic code.
CT Bacteriophage phi X 174: GE, genetics
*Bacteriophages: GE, genetics
Base Composition
Base Sequence
***Codon: AN, analysis**
*DNA, Viral
English Abstract
Genetic Code
***RNA, Messenger: AN, analysis**
Selection (Genetics)
CN 0 (Codon); 0 (DNA, Viral); 0 (**RNA**, Messenger)

L134 ANSWER 120 OF 126 MEDLINE
AN 80254346 MEDLINE
DN 80254346
TI [Possibilities of forming a hydrogen-bonded cytosine-adenine pair in the structure of transfer ribonucleic acid and at the wobble-position of the codon-anticodon complex].
O vozmozhnostiakh obrazovaniia vodorodno-sviazannoi pary tsitozin-adenin v strukture transportnoi ribonukleinovoi kisloty i Wobble-pozitsii kodon-antikodonovogo kompleksa.
AU Mikel'saar R N
SO MOLEKULIARNAIA BIOLOGIIA, **(1980 May-Jun)** 14 (3) 694-707.
Journal code: NGX. ISSN: 0026-8984.
CY USSR
DT Journal; Article; (JOURNAL ARTICLE)
LA Russian
FS Priority Journals
EM 198012
AB 220 nucleotide sequences of tRNAs were investigated to elucidate the frequency of appearance of C-A pairs in their main two-stranded regions, in the positions 26--44 and 15--48. It was supposed, that in the formation of C-A pairs on antiparallel polynucleotide chains the atomic groups--N4-H and -N3 of cytosine make up H-bonds with the groups N7- and H-N6--of adenine. On parallel chains, H-bonds, probably, form -N6-H and --N1 groups

of adenine with N3- and H-N4--of cytosine. The calculation results predicted a significant energy of ineraction between cytosine and adenine. By the investigation of the molecular models it was shown that the formation of H-bonded C-A pairs requires considerable changes of conformation in rebosephosphate chains. In addition a theoretical analysis revealed the possibility of formation of C-A pairs at the wobble-position of codon-anticodon complex. The significance of this nucleotide pair in the processes of genetic coding proved to depend on the **stability** of the codon-anticodon complex, modification of cytosine 34 and structural features of the distant regions of the tRNA.

CT *Adenine
***Anticodon**
Base Composition
Base Sequence
***Codon**
*Cytosine
English Abstract
Hydrogen Bonding
Models, Molecular
Nucleic Acid Conformation
***RNA, Messenger**
***RNA, Transfer**

RN 71-30-7 (Cytosine); 73-24-5 (Adenine); **9014-25-9 (RNA, Transfer)**
CN 0 (Anticodon); 0 (Codon); 0 (**RNA**, Messenger)

L134 ANSWER 121 OF 126 MEDLINE
AN 80144910 MEDLINE
DN 80144910
TI Secondary structure of MS2 phage **RNA** and bias in code word usage.
AU Hasegawa M; Yasunaga T; Miyata T
SO NUCLEIC ACIDS RESEARCH, **(1979 Dec 11)** 7 (7) 2073-9.
Journal code: O8L. ISSN: 0301-5610.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198007
AB Based on the secondary structural model of MS2 **RNA**, it is shown that, in base-pairing regions of the **RNA**, there is a bias in the use of synonymous codons which favours C and/or G over U and/or A in the third codon positions, and that in non-pairing regions, there is an opposite bias which favours U and/or A over C and/or G. This nature is interpreted as a result of selective constraint which **stabilises** the secondary structure of the single-stranded **RNA** genome of the MS2 phage.

CT Base Sequence
***Codon**
*Coliphages: GE, genetics
Nucleic Acid Conformation
***RNA Phages: ME, metabolism**
***RNA, Messenger**
***RNA, Viral**

L134 ANSWER 122 OF 126 MEDLINE
AN 79111929 MEDLINE
DN 79111929
TI Bacteriophage MS2 **RNA**: a correlation between the **stability** of the codon: anticodon interaction and the choice of code words.
AU Grosjean H; Sankoff D; Jou W M; Fiers W; Cedergren R J
SO JOURNAL OF MOLECULAR EVOLUTION, **(1978 Dec 29)** 12 (2) 113-9.
Journal code: J76. ISSN: 0022-2844.
CY GERMANY, WEST: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English

FS Priority Journals
EM 197906
AB The non-random distribution of degenerate code words in Bacteriophage MS2 **RNA** can be explained partially by considerations of the **stability** of the codon-anticodon complex in prokaryotic systems. Supporting this hypothesis we note that wobble codons are positively selected in codons having G and/or C in the first two positions. In contrast, wobble codons are statistically less likely in codons composed of A and U in the first two positions. Analyses of nucleotides adjacent to 5' and 3' ends of codons indicate a nonrandom distribution as well. It is thus likely that some elements of **RNA** evolution are independent of the structural needs of the **RNA** itself and of the translated protein product.
CT ***Anticodon**
***Codon**
*Coliphages: GE, genetics
Escherichia coli: GE, genetics
Genetic Code
***RNA, Messenger**
***RNA, Transfer**
Thermodynamics
Translation, Genetic

L134 ANSWER 123 OF 126 MEDLINE
AN 79024616 MEDLINE
DN 79024616
TI The mechanism of codon-anticodon interaction in ribosomes. Quantitative study of codon-dependent binding of tRNA to the 30-S ribosomal subunits of Escherichia coli.
AU Kirillov S V; Makhno V I; Semenkov Y P
SO EUROPEAN JOURNAL OF BIOCHEMISTRY, **(1978 Aug 15)** 89 (1) 297-304. Journal code: EMZ. ISSN: 0014-2956.
CY GERMANY, WEST: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 197902
AB The formation of a ternary complex 30-S-subunit . poly(U) . tRNAPhe is discussed and the conditions for its correct description by Langmuir's isotherm are deduced. The affinity constant of the binary complex 30-S-subunit . poly(U) is measured. The reversibility of binding of tRNAPhe to the complex 30-S-subunit . poly(U) is proved in a direct way. The main reason for the heterogeneity of ternary complexes was found to be due to the ability of high-molecular-weight poly(U) to form complicated aggregates with 30-S subunits. If a fraction of poly(U) of moderate molecular weight (30 000) is used, then the ternary complexes are homogeneous in **stability** and yield the same affinity constants for deacylated, aminoacylated and peptidyl-tRNAPhe (1 X 10(8) M-1 at 20 mM Mg2+, 200 mM NH+4 and 0 degrees C). Ribosomal protein S1 increases the binding constant of poly(U) with 30-S subunits but does not change the binding constant of tRNAPhe with the 30-S-subunit . poly(U) complex. All 30-S subunits, even partially stripped of S1 protein, are active in the binding of both poly(U) and tRNAPhe.
CT ***Anticodon: ME, metabolism**
***Codon: ME, metabolism**
Escherichia coli: GE, genetics
*Escherichia coli: ME, metabolism
Kinetics
Mathematics
Phenylalanine
Poly U
*Ribosomes: ME, metabolism
***RNA, Messenger: ME, metabolism**
***RNA, Transfer: ME, metabolism**
Translation, Genetic

L134 ANSWER 124 OF 126 MEDLINE
AN 76078435 MEDLINE
DN 76078435
TI Allosteric mechanism for codon-dependent tRNA selection on ribosomes.
AU Kurland C G; Rigler R; Ehrenberg M; Blomberg C
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, **(1975 Nov)** 72 (11) 4248-51.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 197604
AB We suggest that the interaction between a codon and its cognate tRNA induces conformational changes in the tRNA. We further suggest that sites on the ribosome preferentially bind tRNA in those conformations which require proper matching of codon and anticodon. According to this model, the codon functions as an allosteric effector which influences the conformation at various sites in the tRNA. This is made possible by the ribosome, which we suggest traps tRNA molecules in those conformation states that maximize the energy difference between cognate and noncognate codon-anticodon interactions. Studies of the interactions between tRNA molecules and their cognate codons in the absence of the ribosome have suggested that triplet-triplet interaction between codon and anticodon is far too weak to account for the specificity of the tRNA selection mechanism during protein synthesis. In contrast, we suggest that such affinity measurements do not adequately describe the interaction between a codon and its cognate tRNA. Thus, such experiments can not detect conformational changes in the tRNA, and, in particular, those **stabilized** by the ribosome.
CT Allosteric Regulation
Allosteric Site
***Codon: ME, metabolism**
*Models, Biological
Nucleic Acid Conformation
*Ribosomes: ME, metabolism
***RNA, Messenger: ME, metabolism**
***RNA, Transfer: ME, metabolism**
*Translation, Genetic

L134 ANSWER 125 OF 126 MEDLINE
AN 76022314 MEDLINE
DN 76022314
TI A study of codon-dependent binding of aminoacyl-tRNA with the ribosomal 30-S subparticle of Escherichia coli. Determination of the active-particle fraction and binding constants in different media.
AU Glukhova M A; Belitsina N V; Spirin A S
SO EUROPEAN JOURNAL OF BIOCHEMISTRY, **(1975 Mar 3)** 52 (1) 197-202.
Journal code: EMZ. ISSN: 0014-2956.
CY GERMANY, WEST: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 197602
AB Titration of isolated Escherichia coli ribosomal 30-S particles with [14C]phenylalanyl-tRNA in the presence of poly(uridylic acid) was used for a quantitative assay of codon-dependent binding of aminoacyl-tRNA with the small ribosomal subparticle. The technique has allowed the estimation both of the fraction of "active" 30-S subparticles capable of forming the 30-S - poly(U) - phenylalanyl-tRNA complexes and the equilibrium constants of phenylalanyl-tRNA binding in different media. Heterogeneity of the ternary complexes formed has been revealed: at least two classes of complexes differing in **stability** have been observed. The **stability** of the 30-S - poly(U) - phenylalanyl-tRNA complexes has been shown to decrease with the lowering of the Mg2+ concentration, the increase of K+ concentration and the addition of urea. The **stability** of the

complexes increases with the increase of Mg2+ concentration, with the addition of ethanol and decrease of temperature. It is demonstrated that the fraction of actively binding 30-S particles also varies in different medium conditions; it decreases with the increase of ionic strength (K+) and with the addition of urea, and increases with the increase of Mg2+ concentration and addition of ethanol.

CT Binding Sites
***Codon**
**Drug Stability**
*Escherichia coli: ME, metabolism
Ethanol: PD, pharmacology
Kinetics
Macromolecular Systems
Magnesium: PD, pharmacology
Phenylalanine
Poly U
Potassium: PD, pharmacology
Receptors, Drug
Ribosomes: DE, drug effects
*Ribosomes: ME, metabolism
***RNA, Bacterial: ME, metabolism**
***RNA, Messenger**
***RNA, Transfer: ME, metabolism**
Urea: PD, pharmacology

L134 ANSWER 126 OF 126 MEDLINE
AN 75095560 MEDLINE
DN 75095560
TI Protein synthesis in rabbit reticulocytes. A study of Met-tRNA f Mèt binding factor(s) and Met-tRNA f Met binding to ribosomes and AUG codon.
AU Gupta N K; Chatterjee B; Chen Y C; Majumdar A
SO JOURNAL OF BIOLOGICAL CHEMISTRY, **(1975 Feb 10)** 250 (3) 853-62.
Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Cancer Journals; Priority Journals
EM 197506
AB The effects of additions of Mg-2+, ribosomes, and AUG codon on the Met-tRNAf Met-initiation factor-GTP complex were studied using a Millipore filtration method (J. Biol. Chem. 248, 4500 (1973)). Upon addition of increasing concentration of Mg-2+, the Met-tRNAf Met-initiation factor-GTP complex dissociates into free Met-tRNAf Met and initiation factor (GTP), with an infection around 1.5 to 2 mM Mg-2+. The Mg-2+-induced dissociation of Met-tRNAf Met-initiation factor-GTP complex was enhanced at ice bath temperature. At 37 degrees and in the presence of 1.5 to 2mM Mg-2+, the Met-tRNAf Met-initiation factor-GTP complex catalyzes the transfer of Met-tRNAf Met to ribosomes and AUG codon. Ribosome bound Met-tRNAf Met is **stable** to Mg-2+ and low temperature. A Millipore filtration assay for studies of (35S)Met-tRNAf Met binding to ribosomes and Aug codon has been developed. The assay procedure is carried out in three stages. In Stage I, the Met-tRNAf Met is bound to initiation factor in the presence of GTP, AUG codon (required for Stage II reaction), and 3.7 times 10-5 M aurintricarboxylic acid. The incubation is carried out at 37 degrees for 5 min. In Stage II, ribosomes and Mg-2+ (1.5 to 2mM final concentration) are added and the incubation is continued at 37 degrees for 10 min. In Stage III, more Mg-2+ is added to make the final Mg-2+ concentration of the incubation mixture 5 mM, and the reactions are further incubated at ice bath temperature for 10 min. The reactions are then terminated by addition of excess cold wash buffer and filtered through Millipore filters. Under the standard assay conditions, the radioactivity bound to Millipore filters in the absence of ribosomes and AUG codon is markedly reduced. Addition of ribosomes alone gave a significant increase in the radioactivity bound to Millipore filters. A further 2- to 3-fold stimulation of binding of (35S)Met-tRNAf Met to Millipore filters was observed when both ribosomes and AUG codon were added. The Met-tRNAf Met

bound to ribosomes under the assay condition was reactive with puromycin. Upon DEAE-cellulose chromatography of a partially purified mixture of initiation factors (IF), Met-tRNAf Met binding activities separate into two forms, and are designated as IF-1A and IF-1B. These two forms can be distinguished by the **stabilities** of their respective Met-tRNAf Met-IF-1-GTP complexes to Mg-2+. The Met-tRNAf Met-IF-1A-GTP complex is distinctly more **stable** in the presence of Mg-2+ than Met-tRNAf Met-IF-1B-GTP complex. Continue.

CT Check Tags: Animal; Support, U.S. Gov't, P.H.S.
*Blood Proteins: BI, biosynthesis
Centrifugation, Density Gradient
Chromatography, DEAE-Cellulose
***Codon**
Cold
Genetic Code
Guanosine Triphosphate: ME, metabolism
Magnesium: PD, pharmacology
Methionine
Peptide Chain Initiation: DE, drug effects
Peptide Initiation Factors: IP, isolation & purification
***RNA, Messenger**
***RNA, Transfer: ME, metabolism**
Rabbits
Receptors, Drug
*Reticulocytes: ME, metabolism
Ribosomes: DE, drug effects
*Ribosomes: ME, metabolism

RN 86-01-1 (Guanosine Triphosphate); 7439-95-4 (Magnesium); 7005-18-7 (Methionine); **9014-25-9 (RNA, Transfer)**

CN 0 (Blood Proteins); 0 (Codon); 0 (Peptide Initiation Factors); 0 (Receptors, Drug); 0 (**RNA**, Messenger)

=> d all tot

L135 ANSWER 1 OF 37 MEDLINE
AN 1999220879 MEDLINE
DN 99220879
TI alpha-Thalassaemia due to a single codon deletion in the alpha1-globin gene. Computational structural analysis of the new alpha-chain variant. Mutations in brief no. 132. Online.
AU Ayala S; Colomer D; Gelpi J L; Corrons J L
CS Hematology Laboratory Department, Hospital Clinic i Provincial, Faculty of Medicine, University of Barcelona, Spain.
SO HUMAN MUTATION, **(1998)** 11 (5) 412.
Journal code: BRD. ISSN: 1059-7794.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199906
AB A new unstable alpha-globin chain associated with alpha-thalassemia phenotype has been found in a Spanish patient. Molecular analysis of the alpha-globin gene complex using PCR and non-radioactive single-strand conformation analysis, allowed to identify a new mutation in the second exon of the alpha-globin gene. Direct sequencing of the abnormal fragment revealed a 3 bp deletion, which led to the loss of a single codon corresponding to a Lys (K) residue at position 60 or 61 DK60 or DK61. Theoretical structural analysis, performed by computational methods, indicated that the loss of an amino acid residue at this position disturbed the contact region between the B and E-helices, affecting the overall **stability** of the molecule. Therefore, the DK60 and DK61 results in a structurally abnormal alpha-globin chain, not previously described, named Hb Clinic, which leads to the alpha-thalassemia phenotype in the heterozygote patient. No abnormal hemoglobin was detected by

standard electrophoretic procedures, suggesting that this alpha-globin chain variant is so unstable that it may be catabolized immediately after its synthesis. This mutation was confirmed by PCR using an allele specific primer.

CT Check Tags: Case Report; Human; Support, Non-U.S. Gov't
***Codon: GE, genetics**
Computational Biology
*Globin: GE, genetics
*Sequence Deletion: GE, genetics
Spain
*alpha-Thalassemia: GE, genetics
RN 9004-22-2 (Globin)
CN 0 (Codon)

L135 ANSWER 2 OF 37 MEDLINE
AN 1999156225 MEDLINE
DN 99156225
TI Comparison of synonymous codon distribution patterns of bacteriophage and host genomes.
AU Kunisawa T; Kanaya S; Kutter E
CS Department of Applied Biological Sciences, Science University of Tokyo, Noda, Japan.. kunisawa@rs.noda.sut.ac.jp
SO DNA RESEARCH, **(1998 Dec 31)** 5 (6) 319-26.
Journal code: CCB. ISSN: 1340-2838.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199907
EW 19990702
AB Synonymous codon usage patterns of bacteriophage and host genomes were compared. Two indexes, G + C base composition of a gene (fgc) and fraction of translationally **optimal** codons of the gene (fop), were used in the comparison. Synonymous codon usage data of all the coding sequences on a genome are represented as a cloud of points in the plane of fop vs. fgc. The Escherichia coli coding sequences appear to exhibit two phases, "rising" and "flat" phases. Genes that are essential for survival and are thought to be native are located in the flat phase, while foreign-type genes from prophages and transposons are found in the rising phase with a slope of nearly unity in the fgc vs. fop plot. Synonymous codon distribution patterns of genes from temperate phages P4, P2, N15 and lambda are similar to the pattern of E. coli rising phase genes. In contrast, genes from the virulent phage T7 or T4, for which a phage-encoded DNA polymerase is identified, fall in a linear curve with a slope of nearly zero in the fop vs. fgc plane. These results may suggest that the G + C contents for T7, T4 and E. coli flat phase genes are subject to the directional mutation pressure and are determined by the DNA polymerase used in the replication. There is significant variation in the fop values of the phage genes, suggesting an adjustment to gene expression level. Similar analyses of codon distribution patterns were carried out for Haemophilus influenzae, Bacillus subtilis, Mycobacterium tuberculosis and their phages with complete genomic sequences available.

CT Check Tags: Comparative Study
Bacillus subtilis: GE, genetics
Bacteriophage lambda: GE, genetics
Bacteriophage P2: GE, genetics
Bacteriophage T7: GE, genetics
*Bacteriophages: GE, genetics
***Codon: GE, genetics**
Databases, Factual
DNA-Directed DNA Polymerase: GE, genetics
Escherichia coli: GE, genetics
*Genome, Bacterial
*Genome, Viral
Haemophilus influenzae: GE, genetics
Mycobacterium tuberculosis: GE, genetics

Ribosomes: GE, genetics
CN EC 2.7.7.7 (DNA-Directed DNA Polymerase); 0 (Codon)

L135 ANSWER 3 OF 37 MEDLINE
AN 1999036423 MEDLINE
DN 99036423
TI **Optimization** of codon usage of plasmid DNA vaccine is required for the effective MHC class I-restricted T cell responses against an intracellular bacterium.
AU Uchijima M; Yoshida A; Nagata T; Koide Y
CS Department of Microbiology and Immunology, Hamamatsu University School of Medicine, Japan.
SO JOURNAL OF IMMUNOLOGY, **(1998 Nov 15)** 161 (10) 5594-9.
Journal code: IFB. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199902
EW 19990204
AB In an attempt to study codon usage effects of DNA vaccines on the induction of MHC class I-restricted T cell responses against an intracellular bacterium, Listeria monocytogenes, we designed two plasmid DNA vaccines encoding an H-2Kd-restricted epitope of listeriolysin O (LLO) of L. monocytogenes, LLO 91-99. One DNA vaccine, p91wt, carries the wild-type DNA sequence encoding LLO 91-99, and the other one, p91mam, possesses the altered DNA sequence in which the codon usage was **optimized** for murine system. Our read-through analyses with LLO 91-99/luciferase fusion genes confirmed that the **optimized** 91mam DNA sequence showed extremely higher translation efficiency than the wild-type sequence in murine cells. Consistent with this, i.m. injections of p91mam, but not of p91wt, into BALB/c mice were capable of inducing specific CTL- and IFN-gamma-producing CD8+ T cells able to confer partial protection against listerial challenge. Taken together, these observations suggest that **optimization** of codon should be taken into consideration in the construction of DNA vaccines against nonviral pathogens.
CT Check Tags: Animal; Comparative Study; Support, Non-U.S. Gov't
Bacterial Vaccines: GE, genetics
*Bacterial Vaccines: IM, immunology
***Codon: IM, immunology**
Cytokines: BI, biosynthesis
Cytotoxicity, Immunologic
Histocompatibility Antigens Class I: IM, immunology
*Intracellular Fluid: IM, immunology
Intracellular Fluid: MI, microbiology
Listeria monocytogenes: GE, genetics
*Listeria monocytogenes: IM, immunology
Luciferase: GE, genetics
Mice
Mice, Inbred BALB C
Open Reading Frames: GE, genetics
Open Reading Frames: IM, immunology
*Plasmids: IM, immunology
*T-Lymphocyte Subsets: IM, immunology
T-Lymphocyte Subsets: ME, metabolism
T-Lymphocyte Subsets: MI, microbiology
T-Lymphocytes, Cytotoxic: IM, immunology
T-Lymphocytes, Cytotoxic: ME, metabolism
T-Lymphocytes, Cytotoxic: MI, microbiology
Translation, Genetic: IM, immunology
Vaccines, DNA: GE, genetics
*Vaccines, DNA: IM, immunology
CN EC 1.13.12.- (Luciferase); 0 (Bacterial Vaccines); 0 (Codon); 0 (Cytokines); 0 (Histocompatibility Antigens Class I); 0 (Plasmids); 0 (Vaccines, DNA)

L135 ANSWER 4 OF 37 MEDLINE
AN 1998382533 MEDLINE
DN 98382533
TI Codon usage in highly expressed genes of Haemophillus influenzae and Mycobacterium tuberculosis: translational selection versus mutational bias.
AU Pan A; Dutta C; Das J
CS Biophysics Division, Indian Institute of Chemical Biology, 4 Raja S.C. Mullick Road, Calcutta 700032, India.
SO GENE, **(1998 Jul 30)** 215 (2) 405-13.
Journal code: FOP. ISSN: 0378-1119.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199812
EW 19981201
AB Biases in the codon usage and base compositions at three codon sites in different genes of A+T-rich Gram-negative bacterium Haemophillus influenzae and G+C-rich Gram-positive bacterium Mycobacterium tuberculosis have been examined to address the following questions: (1) whether the synonymous codon usage in organisms having highly skewed base compositions is totally dictated by the mutational bias as reported previously (Sharp, P.M., Devine, K.M., 1989. Codon usage and gene expression level in Dictyostelium discoideum: highly expressed genes do 'prefer' **optimal** codons. Nucleic Acids Res. 17, 5029-5039), or is also controlled by translational selection; (2) whether preference of G in the first codon positions by highly expressed genes, as reported in Escherichia coli (Gutierrez, G., Marquez, L., Marin, A., 1996. Preference for guanosine at first codon position in highly expressed Escherichia coli genes. A relationship with translational efficiency. Nucleic Acids Res. 24, 2525-2527), is true in other bacteria; and (3) whether the usage of bases in three codon positions is species-specific. Result presented here show that even in organisms with high mutational bias, translational selection plays an important role in dictating the synonymous codon usage, though the set of **optimal** codons is chosen in accordance with the mutational pressure. The frequencies of G-starting codons are positively correlated to the level of expression of genes, as estimated by their Codon Adaptation Index (CAI) values, in M. tuberculosis as well as in H. influenzae in spite of having an A+T-rich genome. The present study on the codon preferences of two organisms with oppositely skewed base compositions thus suggests that the preference of G-starting codons by highly expressed genes might be a general feature of bacteria, irrespective of their overall G+C contents. The ranges of variations in the frequencies of individual bases at the first and second codon positions of genes of both H. influenzae and M. tuberculosis are similar to those of E. coli, implying that though the composition of all three codon positions is governed by a selection-mutation balance, the mutational pressure has little influence in the choice of bases at the first two codon positions, even in organisms with highly biased base compositions.
CT Check Tags: Animal; Support, Non-U.S. Gov't
Base Composition
***Codon: GE, genetics**
Dictyostelium: GE, genetics
Escherichia coli: GE, genetics
Genes, Bacterial
*Haemophilus influenzae: GE, genetics
*Models, Genetic
*Mutation
*Mycobacterium tuberculosis: GE, genetics
Selection (Genetics)
*Translation, Genetic
CN 0 (Codon)

L135 ANSWER 5 OF 37 MEDLINE
AN 1998299794 MEDLINE
DN 98299794
TI Cytochrome c oxidase deficiency associated with the first stop-codon point mutation in human mtDNA.
AU Hanna M G; Nelson I P; Rahman S; Lane R J; Land J; Heales S; Cooper M J; Schapira A H; Morgan-Hughes J A; Wood N W
CS Neurogenetics Section, University Department of Clinical Neurology, Institute of Neurology, London, WC1N 3BG, United Kingdom.. mhanna@ion.ucl.ac.uk
SO AMERICAN JOURNAL OF HUMAN GENETICS, **(1998 Jul)** 63 (1) 29-36. Journal code: 3IM. ISSN: 0002-9297.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199810
EW 19981003
AB We have identified the first stop-codon point mutation in mtDNA to be reported in association with human disease. A 36-year-old woman experienced episodes of encephalopathy accompanied by lactic acidemia and had exercise intolerance and proximal myopathy. Histochemical analysis showed that 90% of muscle fibers exhibited decreased or absent cytochrome c oxidase (COX) activity. Biochemical studies confirmed a severe isolated reduction in COX activity. Muscle immunocytochemistry revealed a pattern suggestive of a primary mtDNA defect in the COX-deficient fibers and was consistent with either reduced **stability** or impaired assembly of the holoenzyme. Sequence analysis of mtDNA identified a novel heteroplasmic G-->A point mutation at position 9952 in the patient's skeletal muscle, which was not detected in her leukocyte mtDNA or in that of 120 healthy controls or 60 additional patients with mitochondrial disease. This point mutation is located in the 3' end of the gene for subunit III of COX and is predicted to result in the loss of the last 13 amino acids of the highly conserved C-terminal region of this subunit. It was not detected in mtDNA extracted from leukocytes, skeletal muscle, or myoblasts of the patient's mother or her two sons, indicating that this mutation is not maternally transmitted. Single-fiber PCR studies provided direct evidence for an association between this point mutation and COX deficiency and indicated that the proportion of mutant mtDNA required to induce COX deficiency is lower than that reported for tRNA-gene point mutations. The findings reported here represent only the second case of isolated COX deficiency to be defined at the molecular genetic level and reveal a new mutational mechanism in mitochondrial disease.
CT Check Tags: Case Report; Female; Human; Support, Non-U.S. Gov't
Adult
Amino Acid Sequence
***Codon, Terminator: GE, genetics**
*Cytochrome-c Oxidase: DF, deficiency
Cytochrome-c Oxidase: GE, genetics
*DNA, Mitochondrial: GE, genetics
Histocytochemistry
Immunohistochemistry
Mitochondrial Myopathies: GE, genetics
Molecular Sequence Data
Muscle, Skeletal: CY, cytology
Muscle, Skeletal: EN, enzymology
*Point Mutation: GE, genetics
Sequence Analysis, DNA
CN EC 1.9.3.1 (Cytochrome-c Oxidase); 0 (Codon, Terminator); 0 (DNA, Mitochondrial)

L135 ANSWER 6 OF 37 MEDLINE
AN 1998269011 MEDLINE
DN 98269011
TI Translation of the flagellar gene fliO of Salmonella typhimurium from putative tandem starts.

AU Schoenhals G J; Kihara M; Macnab R M
CS Department of Molecular Biophysics and Biochemistry, Yale University, New Haven, Connecticut 06520-8114, USA.
NC AI12202 (NIAID)
SO JOURNAL OF BACTERIOLOGY, **(1998 Jun)** 180 (11) 2936-42.
Journal code: HH3. ISSN: 0021-9193.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199808
EW 19980804
AB The flagellar gene fliO of Salmonella typhimurium can be translated from an AUG codon that overlaps the termination codon of fliN (K. Ohnishi et al., J. Bacteriol. 179:6092-6099, 1997). However, it had been concluded on the basis of complementation analysis that in Escherichia coli a second start codon 60 bp downstream was the authentic one (J. Malakooti et al., J. Bacteriol. 176:189-197, 1994). This raised the possibility of tandem translational starts, such as occur for the chemotaxis gene cheA; this possibility was increased by the existence of a stem-loop sequence covering the second start, a feature also found with cheA. Protein translated from the first start codon was detected regardless of whether the second start codon was present; it was also detected when the stem-loop structure was disrupted or deleted. Translation from the second start codon, either as the natural one (GUG) or as AUG, was not detected when the first start and intervening sequence were intact. Nor was it detected when the first codon was attenuated (by conversion of AUGAUG to AUAAUA; in S. typhimurium there is a second, adjacent, AUG) or eliminated (by conversion to CGCCGC); disruption of the stem-loop structure still did not yield detectable translation from the second start. When the entire sequence up to the second start was deleted, translation from the second start was detected provided the natural codon GUG had been converted to AUG. A fliO null mutant could be fully complemented in swarm assays whenever the first start and intervening sequence were present, regardless of the state of the second start. Reasonably good complementation occurred when the first start and intervening sequence were absent provided the second start was intact, either as AUG or as GUG; thus translation from the GUG codon must have been occurring even though protein levels were too low to be detected. The translated intervening sequence is rather divergent between S. typhimurium and E. coli and corresponds to a substantial cytoplasmic domain prior to the sole transmembrane segment, which is highly conserved; the sequence following the second start begins immediately prior to that transmembrane segment. The significance of the data for FliO is discussed and compared to the equivalent data for CheA. Attention is also drawn to the fact that given an **optimal** ribosome binding site, AUA can serve as a fairly efficient start codon even though it seldom if ever appears to be used in nature.
CT Check Tags: Support, U.S. Gov't, P.H.S.
Amino Acid Sequence
*Bacterial Proteins: GE, genetics
Base Sequence
**Codon, Initiator: CH, chemistry**
***Codon, Initiator: GE, genetics**
Escherichia coli: GE, genetics
Genes, Structural, Bacterial: GE, genetics
Genetic Complementation Test
Molecular Sequence Data
Mutation
Nucleic Acid Conformation
Recombinant Fusion Proteins
*Salmonella typhimurium: GE, genetics
Species Specificity
*Translation, Genetic: GE, genetics
CN 0 (Bacterial Proteins); 0 (Codon, Initiator); 0 (FliO protein); 0 (Recombinant Fusion Proteins)

L135 ANSWER 7 OF 37 MEDLINE
AN 1998191879 MEDLINE
DN 98191879
TI Codon **optimization** of the gene encoding a domain from human type 1 neurofibromin protein results in a threefold improvement in expression level in Escherichia coli.
AU Hale R S; Thompson G
CS Biomolecular Structure Unit, GlaxoWellcome R & D, Stevenage, United Kingdom.
SO PROTEIN EXPRESSION AND PURIFICATION, **(1998 Mar)** 12 (2) 185-8.
Journal code: BJV. ISSN: 1046-5928.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199807
EW 19980705
AB An internal domain from the human type 1 neurofibromin has previously been expressed in Escherichia coli as a fusion with gluthathione S-transferase (GST). The expression level of this protein was lower than expected and so a gene was constructed using the distribution of codons found in highly expressed E. coli proteins. Codons were assigned using a Microsoft Visual Basic computer program to give a distribution similar to those found in genes which are highly expressed in E. coli. The **optimized** gene was then cloned back into the same GST fusion plasmid and it was found that the expression of soluble protein had increased threefold.
CT Check Tags: Comparative Study; Human
Base Sequence
**Codon: CH, chemistry**
***Codon: GE, genetics**
Electrophoresis, Polyacrylamide Gel
Escherichia coli: GE, genetics
*Gene Expression Regulation: GE, genetics
Molecular Sequence Data
Proteins: BI, biosynthesis
Proteins: CH, chemistry
*Proteins: GE, genetics
Recombinant Proteins: BI, biosynthesis
Recombinant Proteins: CH, chemistry
Recombinant Proteins: GE, genetics
Sequence Alignment
CN 0 (neurofibromatosis type 1 protein); 0 (Codon); 0 (Proteins); 0 (Recombinant Proteins)

L135 ANSWER 8 OF 37 MEDLINE
AN 1998127832 MEDLINE
DN 98127832
TI Growth phase dependent stop codon readthrough and shift of translation reading frame in Escherichia coli.
AU Wenthzel A M; Stancek M; Isaksson L A
CS Department of Microbiology, Stockholm University, Sweden.
SO FEBS LETTERS, **(1998 Jan 16)** 421 (3) 237-42.
Journal code: EUH. ISSN: 0014-5793.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199805
EW 19980501
AB Nonsense codon readthrough and changed translational reading frame were measured in different growth phases in E. coli. The strains used carry plasmid constructs with a translation assay reporter gene. This reporter gene contains an internal stop codon or a run of U-residues. Termination or frameshifting give rise to **stable** proteins that can be physically quantified on gels along with the complete protein products. Readthrough of the stop codon UGA by a nearcognate tRNA is several fold

higher in active growth than in late exponential phase. In early exponential phase, about 7% of -1 frameshift at a U9 slippery sequence is detectable; upon entry to stationary phase this frameshifting increases to about 40% followed by a decrease in stationary phase. A similar increase is observed in the case of +1 reading frameshift at the U9 sequence, which increases from 13% in early exponential growth phase up to 38% at the beginning of stationary phase followed by a decrease. Thus, the levels of both stop codon readthrough and frameshifting are growth phase dependent, though not in an identical fashion.

CT Check Tags: Support, Non-U.S. Gov't
Base Sequence
***Codon, Terminator**
DNA, Bacterial
Escherichia coli: GD, growth & development
*Escherichia coli: GE, genetics
*Frameshifting, Ribosomal
Molecular Sequence Data
*Reading Frames

CN 0 (Codon, Terminator); 0 (DNA, Bacterial)

L135 ANSWER 9 OF 37 MEDLINE
AN 1998088583 MEDLINE
DN 98088583
TI Missense mutations in codon 225 of ornithine transcarbamylase (OTC) result in decreased amounts of OTC protein: a hypothesis on the molecular mechanism of the OTC deficiency.
AU Garcia-Perez M A; Climent C; Briones P; Vilaseca M A; Rodes M; Rubio V
CS Instituto de Investigaciones Citologicas, Fundacion Valenciana de Investigaciones Biomedicas, Valencia, Spain.
SO JOURNAL OF INHERITED METABOLIC DISEASE, **(1997 Nov)** 20 (6) 769-77.
Journal code: KY8. ISSN: 0141-8955.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199804
EW 19980403
AB Mutations P225L and P225R were identified in codon 225 of the gene for ornithine transcarbamylase (OTC) in two patients with the neonatal form of OTC deficiency. The mutations occur at a CpG dinucleotide and eliminate a unique MspI restriction site in exon 7 of the OTC gene. They do not alter existing splice sites or create new sites, as judged from the nucleotide sequence. Both mutations are associated with undetectable levels of OTC antigen in liver homogenates, and with either complete lack of OTC activity (P225R mutation) or very small residual activity (0.15% of normal in the P225L mutation). The residual activity observed with P225L exhibits normal pH dependence, little or no increases in the Km values for ornithine and carbamoyl phosphate and normal **stability** at either 37 degrees C or, in the presence of 0.66 mol/L urea, at 0 degree C. The latter conditions were used to examine whether the P225L mutation favours dissociation of the active OTC trimer. Given the normal **stability** and lack of tendency to dissociation of the mutant enzyme, it appears likely that the dramatic reduction in the level of OTC protein is due to inefficient conversion of the mutant OTC precursor polypeptide (pOTC) into the correctly localized, appropriately folded, mature enzyme trimer, suggesting degradation of pOTC in transit to the mitochondria.

CT Check Tags: Animal; Case Report; Human; Support, Non-U.S. Gov't
Base Sequence
***Codon**
Deoxyribonuclease HpaII: ME, metabolism
**Enzyme Stability**
Exons
Hydrogen-Ion Concentration
Infant, Newborn
Leucine: GE, genetics

Liver: EN, enzymology
Mice
Molecular Sequence Data
*Mutation
*Ornithine Carbamoyltransferase: DF, deficiency
*Ornithine Carbamoyltransferase: GE, genetics
Polymerase Chain Reaction
Proline: GE, genetics
Rats
Sequence Analysis, DNA
RN 147-85-3 (Proline); 7005-03-0 (Leucine)
CN EC 2.1.3.3 (Ornithine Carbamoyltransferase); EC 3.1.21.- (Deoxyribonuclease HpaII); 0 (Codon)

L135 ANSWER 10 OF 37 MEDLINE
AN 97469617 MEDLINE
DN 97469617
TI Effects of codon usage and vector-host combinations on the expression of spinach plastocyanin in Escherichia coli.
AU Ejdeback M; Young S; Samuelsson A; Karlsson B G
CS Department of Biochemistry and Biophysics, Goteborg University, Sweden.
SO PROTEIN EXPRESSION AND PURIFICATION, **(1997 Oct)** 11 (1) 17-25.
Journal code: BJV. ISSN: 1046-5928.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199801
AB Spinach plastocyanin has been expressed in Escherichia coli and exported to the periplasmic space. The effects of codon usage, expression system, growth length, and temperature on expression levels in LB medium were investigated. A stretch of codons, rare in E. coli, was identified and replaced with highly expressed codons, increasing the yield by at least 20%. Plastocyanin was more efficiently expressed under the T7 promoter than under the lac promoter. Maximum yields were obtained at 37 degrees C when growing the cells for 16 h after induction. The **optimized** expression system produced 38 mg holoprotein per liter culture. In this system it was also possible to express plastocyanin in minimal medium, at a yield of 10 mg per liter. N-terminal sequencing and mass spectrometry showed that plastocyanin was correctly processed. The expressed plastocyanin was purified to homogeneity, as shown by an A278/A597 ratio of 1.0, and together with amino acid analysis and the determination of oxidized and total copper contents, both the absorption coefficients for epsilon 278 and for epsilon 597 were determined to be 4700 M-1 cm-1.
CT Check Tags: Support, Non-U.S. Gov't
Amino Acid Sequence
Base Sequence
Cloning, Molecular: MT, methods
***Codon**
Electron Spin Resonance Spectroscopy
*Escherichia coli: GE, genetics
Gene Expression
Molecular Sequence Data
Plastocyanin: BI, biosynthesis
*Plastocyanin: GE, genetics
Recombinant Proteins: BI, biosynthesis
Recombinant Proteins: GE, genetics
Spectrophotometry, Atomic Absorption
*Spinach: GE, genetics
RN 9014-09-9 (Plastocyanin)
CN 0 (Codon); 0 (Recombinant Proteins)

L135. ANSWER 11 OF 37 MEDLINE
AN 97465509 MEDLINE
DN 97465509
TI A dinucleotide deletion results in defective membrane anchoring and

circulating soluble glycoprotein Ib alpha in a novel form of Bernard-Soulier syndrome.

AU Kenny D; Newman P J; Morateck P A; Montgomery R R
CS Department of Medicine, Medical College of Wisconsin, Milwaukee, USA.

NC R29 HL56027 (NHLBI)
PO1 HL44612 (NHLBI)
RR0344 (NCRR)
SO BLOOD, **(1997 Oct 1)** 90 (7) 2626-33.
Journal code: A8G. ISSN: 0006-4971.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199801
EW 19980104

AB The platelet membrane glycoprotein (GP)Ib-V-IX complex is the receptor for von Willebrand factor and is composed of four membrane-spanning polypeptides: GPIb alpha, GPIb beta, GPIX, and GPV. A qualitative or quantitative deficiency in the GPIb-V-IX complex on the platelet membrane is the cause of the congenital platelet disorder Bernard-Soulier syndrome (BSS). We describe the molecular basis of a novel variant BSS in a patient in which GPIb alpha was absent from the platelet surface but present in a soluble form in the plasma. DNA sequence analysis showed a homozygous dinucleotide deletion in the codon for Tyr 508 (TAT) in GPIb alpha. This mutation (GPIb alpha deltaAT) causes a frame shift that alters the amino acid sequence of GPIb alpha within its transmembrane region. The hydrophobic nature of the predicted transmembrane region and the cytoplasmic tail at the COOH terminal are altered before reaching a new premature stop codon 38 amino acids short of the wild-type peptide. Although GPIb alpha deltaAT was not detectable on the platelet surface, immunoprecipitation of plasma with specific monoclonal antibodies (MoAbs) identified circulating GPIb alpha. Transient expression of recombinant GPIb alpha deltaAT in 293T cells also generated a soluble form of the protein. Moreover, when a plasmid encoding GPIb alpha deltaAT was transiently transfected into Chinese hamster ovary (CHO) cells **stably** expressing the GP beta-IX complex, it failed to be expressed on the cell surface. Thus, a dinucleotide deletion in the codon for Tyr 508 causes a frameshift that alters the amino acid sequence of GPIb alpha starting within its transmembrane region, changes the hydrophobicity of the normal transmembrane region, and truncates the cytoplasmic domain affecting binding to the cytoskeleton and cytoplasmic proteins. This mutation affects anchoring of the GPIb alpha polypeptide in platelets and causes the observed BSS phenotype with circulating soluble GPIb alpha.

CT Check Tags: Animal; Case Report; Female; Human; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.

Aged
Amino Acid Sequence
Bernard-Soulier Syndrome: BL, blood
*Bernard-Soulier Syndrome: GE, genetics
*Blood Platelets: ME, metabolism
*Cell Membrane: ME, metabolism
***Codon: GE, genetics**
Cricetulus
Cytoplasm: ME, metabolism
Cytoskeleton: ME, metabolism
CHO Cells
DNA Mutational Analysis
Hamsters
Molecular Sequence Data
*Platelet Glycoprotein GPIb-IX Complex: ME, metabolism
Polymerase Chain Reaction
Protein Binding
Protein Structure, Secondary
Recombinant Fusion Proteins: ME, metabolism
*Sequence Deletion

CN 0 (Codon); 0 (Platelet Glycoprotein GPIb-IX Complex); 0 (Recombinant Fusion Proteins)

L135 ANSWER 12 OF 37 MEDLINE
AN 97368269 MEDLINE
DN 97368269
TI Evolution of codon usage bias in Drosophila.
AU Powell J R; Moriyama E N
CS Department of Ecology and Evolutionary Biology, Yale University, New Haven, CT 06520-8106, USA.. jeffrey.powell@yale.edu
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, **(1997 Jul 22)** 94 (15) 7784-90.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199710
EW 19971005
AB We first review what is known about patterns of codon usage bias in Drosophila and make the following points: (i) Drosophila genes are as biased or more biased than those in microorganisms. (ii) The level of bias of genes and even the particular pattern of codon bias can remain phylogenetically invariant for very long periods of evolution. (iii) However, some genes, even very tightly linked genes, can change very greatly in codon bias across species. (iv) Generally G and especially C are favored at synonymous sites in biased genes. (v) With the exception of aspartic acid, all amino acids contribute significantly and about equally to the codon usage bias of a gene. (vi) While most individual amino acids that can use G or C at synonymous sites display a preference for C, there are exceptions: valine and leucine, which prefer G. (vii) Finally, smaller genes tend to be more biased than longer genes. We then examine possible causes of these patterns and discount mutation bias on three bases: there is little evidence of regional mutation bias in Drosophila, mutation bias is likely toward A+T (the opposite of codon usage bias), and not all amino acids display the preference for the same nucleotide in the wobble position. Two lines of evidence support a selection hypothesis based on tRNA pools: highly biased genes tend to be highly and/or rapidly expressed, and the preferred codons in highly biased genes **optimally** bind the most abundant isoaccepting tRNAs. Finally, we examine the effect of bias on DNA evolution and confirm that genes with high codon usage bias have lower rates of synonymous substitution between species than do genes with low codon usage bias. Surprisingly, we find that genes with higher codon usage bias display higher levels of intraspecific synonymous polymorphism. This may be due to opposing effects of recombination.
CT Check Tags: Animal; Support, U.S. Gov't, Non-P.H.S.
***Codon**
*Drosophila: GE, genetics
*Evolution, Molecular
Recombination, Genetic
CN 0 (Codon)

L135 ANSWER 13 OF 37 MEDLINE
AN 97345667 MEDLINE
DN 97345667
TI Bacterial expression and purification of biologically active mouse c-Fos proteins by selective codon **optimization**.
AU Deng T
CS Department of Biochemistry and Molecular Biology, College of Medicine, University of Florida, Gainesville 32610-0245, USA.. tdeng@biochem.med.ufl.edu
SO FEBS LETTERS, **(1997 Jun 9)** 409 (2) 269-72.
Journal code: EUH. ISSN: 0014-5793.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)

LA English
FS Priority Journals; Cancer Journals
EM 199709
EW 19970903
AB A simple strategy using selective codon **optimization** was devised to express mouse c-Fos protein in high levels in E. coli. Ten arginine codons located in the basic region were **optimized** to achieve high levels of protein expression. The c-Fos protein was purified to near homogeneity and was demonstrated to be biologically active by assaying its several biological activities.
CT Check Tags: Animal; Support, Non-U.S. Gov't
Arginine: GE, genetics
***Codon: GE, genetics**
Electrophoresis, Polyacrylamide Gel
Escherichia coli: GE, genetics
*Genetic Vectors: ME, metabolism
Mice
Mutagenesis, Insertional
*Proto-Oncogene Proteins c-fos: BI, biosynthesis
*Proto-Oncogene Proteins c-fos: GE, genetics
Proto-Oncogene Proteins c-fos: IP, isolation & purification
RN 7004-12-8 (Arginine)
CN 0 (Codon); 0 (Genetic Vectors); 0 (Proto-Oncogene Proteins c-fos)

L135 ANSWER 14 OF 37 MEDLINE
AN 97276224 MEDLINE
DN 97276224
TI Further characterization of HLA homozygous typing cell lines at the LMP2 polymorphic codon 60 by an ARMS typing method.
AU Hopkins L M; Bull P J; Gerlach J A; Bull R W
CS Immunohematology and Serology Laboratory, Michigan State University, East Lansing 48824, USA.
SO HUMAN IMMUNOLOGY, **(1997 Apr 1)** 53 (2) 183-7.
Journal code: G9W. ISSN: 0198-8859.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199708
EW 19970804
AB LMP2 is a subunit of the 20S proteasome within the cellular cytosolic compartment that is thought to cleave proteins into approximately 9 amino acid long oligopeptides. It is hypothesized that changes in the low molecular mass protease (LMP) gene sequence may alter the activity or specificity in which the LMP genes cleave peptides. Currently, the typing method for LMP2 involves polymerase chain reaction (PCR), restriction enzyme digestion, and gel electrophoresis. To help reduce the cost and cumbersomeness of this method, a new typing method was adapted for the LMP2 gene. To establish this new amplification refractory mutation system (ARMS) typing method, primers have been defined, amplification conditions **optimized**, and control cell lines sequenced to validate testing parameters. Results are listed for selected 10th and 11th International Histocompatibility Workshop homozygous cell lines.
CT Check Tags: Human; Support, Non-U.S. Gov't
Cell Line
***Codon: GE, genetics**
DNA Primers
Genotype
*Histocompatibility Testing: MT, methods
Homozygote
*HLA Antigens: GE, genetics
*Polymerase Chain Reaction: MT, methods
*Polymorphism (Genetics)
*Proteins: GE, genetics
RN 144416-78-4 (LMP-2 protein)
CN 0 (Codon); 0 (DNA Primers); 0 (HLA Antigens); 0 (Proteins)

L135 ANSWER 15 OF 37 MEDLINE
AN 97118940 MEDLINE
DN 97118940
TI Expression and codon usage **optimization** of the erythroid-specific transcription factor cGATA-1 in baculoviral and bacterial systems.
AU Pikaart M J; Felsenfeld G
CS Laboratory of Molecular Biology, National Institute of Diabetes and Digestion and Kidney Disease, National Institutes of Health, Bethesda, Maryland 20892-0540, USA.
SO PROTEIN EXPRESSION AND PURIFICATION, **(1996 Dec)** 8 (4) 469-75.
Journal code: BJV. ISSN: 1046-5928.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199705
EW 19970504
AB Biochemical characterization of cGATA-1, a key transcription factor in the regulation of globin expression in chickens, has been precluded by the unavailability of appreciable amounts of the pure protein. Purification directly from embryonic red blood cells has been limited by the difficulty in obtaining large quantities of the starting material, and previous attempts at bacterial expression have consistently yielded truncated product. To solve these problems, we have taken two approaches to the expression of cGATA-1. First, we were able to produce efficient expression from baculovirus-infected insect cells. Second, by altering the codon usage in cDNA encoding the protein's carboxy-terminal region, we obtained good expression of full-length protein in Escherichia coli. These preparations should prove useful in biochemical and structural studies of the factor. Additionally, we describe a primer extension/PCR-based method which can be used to synthesize extended regions of DNA sequence for gene construction.
CT Check Tags: Animal
Baculoviridae
Base Sequence
***Codon**
Deoxyribonuclease EcoRI: ME, metabolism
DNA-Binding Proteins: CH, chemistry
*DNA-Binding Proteins: GE, genetics
Genetic Vectors
Molecular Sequence Data
Nuclear Proteins: CH, chemistry
*Nuclear Proteins: GE, genetics
Restriction Mapping
Spodoptera
Transcription Factors: CH, chemistry
*Transcription Factors: GE, genetics
*Zinc Fingers
RN 125267-48-3 (erythroid-specific DNA-binding factor)
CN EC 3.1.21.- (Deoxyribonuclease EcoRI); 0 (Codon); 0 (DNA-Binding Proteins); 0 (Genetic Vectors); 0 (Nuclear Proteins); 0 (Transcription Factors)

L135 ANSWER 16 OF 37 MEDLINE
AN 97105906 MEDLINE
DN 97105906
TI **Optimized** codon usage and chromophore mutations provide enhanced sensitivity with the green fluorescent protein.
AU Yang T T; Cheng L; Kain S R
CS Cell Biology Group, CLONTECH Laboratories Inc., Palo Alto, CA 94303-4230, USA.
SO NUCLEIC ACIDS RESEARCH, **(1996 Nov 15)** 24 (22) 4592-3.
Journal code: O8L. ISSN: 0305-1048.
CY ENGLAND: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199703
AB The green fluorescent protein (GFP) from Aequorea victoria is a versatile reporter protein for monitoring gene expression and protein localization in a variety of cells and organisms. Despite many early successes using this reporter, wild type GFP is suboptimal for most applications due to low fluorescence intensity when excited by blue light (488 nm), a significant lag in the development of fluorescence after protein synthesis, complex photoisomerization of the GFP chromophore and poor expression in many higher eukaryotes. To improve upon these qualities, we have combined a mutant of GFP with a significantly larger extinction coefficient for excitation at 488 nm with a re-engineered GFP gene sequence containing codons preferentially found in highly expressed human proteins. The combination of improved fluorescence intensity and higher expression levels yield an enhanced GFP which provides greater sensitivity in most systems.
CT Check Tags: Animal; Human
Cell Line
***Codon**
CHO Cells
Flow Cytometry
Fluorescence
Hamsters
Jellyfish
*Luminescent Proteins: GE, genetics
RN 147336-22-9 (green fluorescent protein)
CN 0 (Codon); 0 (Luminescent Proteins)

L135 ANSWER 17 OF 37 MEDLINE
AN 97090410 MEDLINE
DN 97090410
TI Codon usage in the Mycobacterium tuberculosis complex.
AU Andersson G E; Sharp P M
CS Department of Molecular Biology, Uppsala University, Sweden.
SO MICROBIOLOGY, **(1996 Apr)** 142 ( Pt 4) 915-25.
Journal code: BXW. ISSN: 1350-0872.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199703
EW 19970301
AB The usage of alternative synonymous codons in Mycobacterium tuberculosis (and M. bovis) genes has been investigated. This species is a member of the high-G+C Gram-positive bacteria, with a genomic G+C content around 65 mol%. This G+C-richness is reflected in a strong bias towards C- and G-ending codons for every amino acid: overall, the G+C content at the third positions of codons is 83%. However, there is significant variation in codon usage patterns among genes, which appears to be associated with gene expression level. From the variation among genes, putative **optimal** codons were identified for 15 amino acids. The degree of bias towards **optimal** codons in an M. tuberculosis gene is correlated with that in homologues from Escherichia coli and Bacillus subtilis. The set of selectively favoured codons seems to be quite highly conserved between M. tuberculosis and another high-G+C Gram-positive bacterium, Corynebacterium glutamicum, even though the genome and overall codon usage of the latter are much less G+C-rich.
CT Check Tags: Comparative Study; Support, Non-U.S. Gov't
Bacillus subtilis: GE, genetics
Base Composition
Base Sequence
***Codon: GE, genetics**
Corynebacterium: GE, genetics
DNA, Bacterial: CH, chemistry

DNA, Bacterial: GE, genetics
Escherichia coli: GE, genetics
Evolution, Molecular
Gene Expression
Genes, Bacterial
Mycobacterium bovis: GE, genetics
*Mycobacterium tuberculosis: GE, genetics
Species Specificity
CN 0 (Codon); 0 (DNA, Bacterial)

L135 ANSWER 18 OF 37 MEDLINE
AN 97025696 MEDLINE
DN 97025696
TI Rare pre-core stop-codon mutant nt. 1897 predominates over wide-spread mutant nt. 1896 in an unusual course of chronic hepatitis B.
AU Protzer U; Trippler M; Ohl J; Knolle P; Duchmann R; Meyer zum Buschenfelde K H; Gerken G
CS Medizinische Klinik and Poliklinik, Johannes-Gutenberg-Universitat, Mainz, Germany.
SO JOURNAL OF VIRAL HEPATITIS, **(1996 May)** 3 (3) 155-62.
Journal code: CG0. ISSN: 1352-0504.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199703
EW 19970302
AB We present a patient with an unusual course of hepatitis B e antigen (HBeAg)-negative chronic hepatitis B who had repeated reactivations of his disease progressing to cirrhosis with terminal liver failure. Each flare up presented like an acute hepatitis with very high titres of hepatitis B virus (HBV) and high inflammatory activity followed by rapid clearance of viraemia. The pre-core genome of HBV isolated from sera during 5 years of follow up was analysed. Direct sequencing of polymerase chain reaction (PCR) products derived from consecutive sera showed a rare pre-core stop-codon mutation at nucleotide (nt.) 1897 G --> A with an accompanying mutation nt. 1857 C --> T as well as a stop-codon mutation nt. 1896 G --> A. By cloning and sequencing of PCR products the mutant strain with mutation nt. 1897 was shown to predominate over viral strains with a mutation nt. 1896 during the course of disease, although the stop-codon mutation nt. 1896 in general is observed more frequently. Both mutations allow viral replication by **stabilizing** the encapsidation signal 'epsilon'. This allowed HBV replication at a very high level as observed during flare ups. The absence of HBeAg may be responsible for the massive cytotoxic T-cell response towards hepatocytes which might explain the rapid progression to liver cirrhosis although no, or very little, HBV replication was observed for long periods. However, there is no clear explanation as to why the nt. 1897 mutant strain overwhelmed the other virus strains.
CT Check Tags: Case Report; Human; Male; Support, Non-U.S. Gov't
Adult
Base Sequence
Chronic Disease
***Codon, Terminator: GE, genetics**
DNA, Viral: AN, analysis
*Hepatitis B: GE, genetics
Hepatitis B e Antigens: AN, analysis
Hepatitis B e Antigens: IM, immunology
Hepatitis B Antibodies: AN, analysis
*Hepatitis B Core Antigens: GE, genetics
Hepatitis B Core Antigens: IM, immunology
Hepatitis B Surface Antigens: AN, analysis
Hepatitis B Surface Antigens: IM, immunology
*Hepatitis B Virus: GE, genetics
Hepatitis B Virus: IM, immunology
Liver: PA, pathology

Liver Failure: VI, virology
Molecular Sequence Data
Mutation
Polymerase Chain Reaction
Signal Transduction: GE, genetics
T-Lymphocytes, Cytotoxic: VI, virology
CN 0 (Codon, Terminator); 0 (DNA, Viral); 0 (Hepatitis B e Antigens); 0 (Hepatitis B Antibodies); 0 (Hepatitis B Core Antigens); 0 (Hepatitis B Surface Antigens)

L135 ANSWER 19 OF 37 MEDLINE
AN 96434046 MEDLINE
DN 96434046
TI PICDI, a simple program for codon bias calculation.
AU Rodriguez-Belmonte E; Freire-Picos M A; Rodriguez-Torres A M; Gonzalez-Siso M I; Cerdan M E; Rodriguez-Seijo J M
CS Departamento de Biologia Celular y Molecular, Facultad de Ciencias, La Coruna, Spain.
SO MOLECULAR BIOTECHNOLOGY, **(1996 Jun)** 5 (3) 191-5.
Journal code: B97. ISSN: 1073-6085.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199702
EW 19970204
AB PICDI is a very simple program designed to calculate the Intrinsic Codon Deviation Index (ICDI). The program is available in Macintosh as well a PC format. Requirements for correct input of the sequences have been kept to a minimum and the analysis of sequences up to 2000 codons is very quick. The ICDI is very useful for estimation of codon bias of genes from species in which **optimal** codons are not known. The availability of a computer program for its calculation will increase its usefulness in the fields of Molecular Biology and Biotechnology.
CT Check Tags: Support, Non-U.S. Gov't
***Codon**
*Database Management Systems
Microcomputers
CN 0 (Codon)

L135 ANSWER 20 OF 37 MEDLINE
AN 96133216 MEDLINE
DN 96133216
TI Autosomal dominant cone-rod dystrophy associated with mutations in codon 244 (Asn244His) and codon 184 (Tyr184Ser) of the peripherin/RDS gene.
AU Nakazawa M; Kikawa E; Chida Y; Wada Y; Shiono T; Tamai M
CS Department of Ophthalmology, Tohoku University School of Medicine, Sendai, Japan.
SO ARCHIVES OF OPHTHALMOLOGY, **(1996 Jan)** 114 (1) 72-8.
Journal code: 830. ISSN: 0003-9950.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199604
AB OBJECTIVE: To characterize clinical findings associated with mutations in codon 244 (Asn244His) and codon 184 (Tyr184Ser) of the peripherin/RDS gene. DESIGN: Case reports with clinical features and results of fluorescein angiography, electroretinography, kinetic visual field testing, and DNA analysis. SETTING: University medical center. PATIENTS: Four affected members of two Japanese families with autosomal dominant cone-rod dystrophy associated with transversion mutations in codon 244 (Asn244His) and codon (Tyr184Ser) of the peripherin/RDS gene. RESULTS: Characteristic features included the initial symptoms of decreased visual acuity, macular degeneration, central or paracentral scotoma, cone-mediated electroretinographic responses that were more impaired than

rod-mediated responses, and pigmentary degeneration in the midperipheral retina in the late stage. These phenotypic features corresponded to cone-rod dystrophy type 2a by the classification of Szlyk and associates. CONCLUSIONS: The Asn244His and Tyr184Ser mutations in the peripherin/RDS gene cause con-rod dystrophy type 2a. These findings imply that a mutation in codon 244 or codon 184 of the peripherin/RDS gene affects the functions and/or structural **stability** of cones and rods.

CT Check Tags: Case Report; Female; Human; Male; Support, Non-U.S. Gov't
Adult
Aged
Amino Acid Sequence
Asparagine
Base Sequence
***Codon: GE, genetics**
DNA: AN, analysis
Electroretinography
*Eye Proteins: GE, genetics
Fluorescein Angiography
Histidine
*Intermediate Filament Proteins: GE, genetics
Membrane Glycoproteins: GE, genetics
Middle Age
Molecular Sequence Data
Pedigree
*Photoreceptors: PA, pathology
*Point Mutation
Polymorphism, Single-Stranded Conformational
*Retinal Degeneration: GE, genetics
Retinal Degeneration: PA, pathology
Serine
Tyrosine
Visual Fields

RN 55520-40-6 (Tyrosine); 56-45-1 (Serine); 7006-34-0 (Asparagine); 7006-35-1 (Histidine); 9007-49-2 (DNA)

CN 0 (peripherin); 0 (Codon); 0 (Eye Proteins); 0 (Intermediate Filament Proteins); 0 (Membrane Glycoproteins)

L135 ANSWER 21 OF 37 MEDLINE

AN 96120355 MEDLINE

DN 96120355

TI Synonymous substitution rates in enterobacteria.

AU Eyre-Walker A; Bulmer M

CS Department of Biological Sciences, Rutgers University, Piscataway, New Jersey 08855-1059, USA.

SO GENETICS, **(1995 Aug)** 140 (4) 1407-12.
Journal code: FNH. ISSN: 0016-6731.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199603

AB It has been shown previously that the synonymous substitution rate between Escherichia coli and Salmonella typhimurium is lower in highly than in weakly expressed genes, and it has been suggested that this is due to stronger selection for translational efficiency in highly expressed genes as reflected in their greater codon usage bias. This hypothesis is tested here by comparing the substitution rate in codon families with different patterns of synonymous codon use. It is shown that the decline in the substitution rate across expression levels is as great for codon families that do not appear to be subject to selection for translational efficiency as for those that are. This implies that selection on translational efficiency is not responsible for the decline in the substitution rate across genes. It is argued that the most likely explanation for this decline is a decrease in the mutation rate. It is also shown that a simple evolutionary model in which synonymous codon use is determined by a balance between mutation, selection for an **optimal** codon, and

genetic drift predicts that selection should have little effect on the substitution rate in the present case.
CT ***Codon: GE, genetics**
*Enterobacteriaceae: GE, genetics
Escherichia coli: GE, genetics
Evolution, Molecular
Gene Frequency
*Models, Genetic
*Mutation
Salmonella typhimurium: GE, genetics
Selection (Genetics)
Sequence Alignment
*Translation, Genetic
CN 0 (Codon)

L135 ANSWER 22 OF 37 MEDLINE
AN 95147464 MEDLINE
DN 95147464
TI Third codon G + C periodicity as a possible signal for an "internal" selective constraint.
AU Lio P; Ruffo S; Buiatti M
CS Dipartimento di Biologia Animale e Genetica, Universita di Firenze, Italy..
SO JOURNAL OF THEORETICAL BIOLOGY, **(1994 Nov 21)** 171 (2) 215-23. Journal code: K8N. ISSN: 0022-5193.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199505
AB Quasi-local analysis methods, such as window Fast Fourier Transform and an information theoretical quantity known as mutual information, have allowed us to gain some further insights on the importance and the contextual dependence of a pattern found in DNA sequences showing a periodicity of three with a G or C base in the third position. We have screened for such a periodicity, in terms of the alternative "strong" (S = C or G) versus "weak" (W = A or T) base, a large sample of DNA coding and non-coding sequences from both prokaryotes and eukaryotes, with the aim of testing whether this pattern could be considered as a significant signal for past or present constraints regarding DNA organization and/or function. This periodicity was indeed found in a number of sequences always associated with open reading frames, generally confined in prokaryotes living in extreme environments or in highly conserved eukaryotic genes. Moreover, codon usage was found to be very similar even in genes coding for very different functions. The data are discussed in view of their possible implications for an adaptive value of such a periodicity, in terms of more accurate translation processing and better overall **stability**.
CT Check Tags: Animal; Human
*Base Sequence
***Codon: GE, genetics**
*Computer Simulation
Genes, Plant
Genetic Code
*Models, Genetic
Reading Frames
*Sequence Analysis, DNA
CN 0 (Codon)

L135 ANSWER 23 OF 37 MEDLINE
AN 95115058 MEDLINE
DN 95115058
TI Translational inhibition by a human cytomegalovirus upstream open reading frame despite inefficient utilization of its AUG codon.
AU Cao J; Geballe A P
CS Department of Molecular Medicine, Fred Hutchinson Cancer Research Center, Seattle, Washington 98104..

NC AI26672 (NIAID)
SO JOURNAL OF VIROLOGY, **(1995 Feb)** 69 (2) 1030-6.
Journal code: KCV. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199504
AB The second of three short upstream open reading frames (uORF2) in the transcript leader of the human cytomegalovirus gp48 (gpUL4) virion glycoprotein gene inhibits downstream translation approximately 10-fold. Remarkably, this inhibition depends on the amino acid coding information of uORF2. In the current studies we demonstrate that expression of the cistron downstream from uORF2 depends on ribosomes bypassing the uORF2 AUG codon (AUG2) by a leaky scanning mechanism. Replacing the nucleotides surrounding the wild-type AUG2 codon with those **optimal** for translation initiation reduces downstream translation approximately 10-fold. Analyses of mutants in which uORF2 either overlaps or is in frame with the downstream reading frame reveal that the initiation frequency at the wild-type AUG2 codon is surprisingly low; rather, the majority of ribosomal subunits bypass the wild-type AUG2 codon because of its suboptimal context. We propose a model to explain this unprecedented example of a paradoxically strong inhibitory effect of an upstream ORF despite inefficient utilization of its initiation codon.
CT Check Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
beta-Galactosidase: GE, genetics
Base Sequence
***Codon**
*Cytomegalovirus: GE, genetics
Molecular Sequence Data
*Open Reading Frames
Signal Peptides: PH, physiology
*Translation, Genetic
*Viral Envelope Proteins: GE, genetics
Viral Envelope Proteins: PH, physiology
CN EC 3.2.1.23 (beta-Galactosidase); 0 (cytomegalovirus glycoprotein 48); 0 (Codon); 0 (Signal Peptides); 0 (Viral Envelope Proteins)

L135 ANSWER 24 OF 37 MEDLINE
AN 94316481 MEDLINE
DN 94316481
TI Codon usage in Caenorhabditis elegans: delineation of translational selection and mutational biases.
AU Stenico M; Lloyd A T; Sharp P M
CS Department of Genetics, Trinity College, Dublin, Ireland..
SO NUCLEIC ACIDS RESEARCH, **(1994 Jul 11)** 22 (13) 2437-46.
Journal code: O8L. ISSN: 0305-1048.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-Z19555; GENBANK-Z19152; GENBANK-L07144
EM 199410
AB Synonymous codon usage varies considerably among Caenorhabditis elegans genes. Multivariate statistical analyses reveal a single major trend among genes. At one end of the trend lie genes with relatively unbiased codon usage. These genes appear to be lowly expressed, and their patterns of codon usage are consistent with mutational biases influenced by the neighbouring nucleotide. At the other extreme lie genes with extremely biased codon usage. These genes appear to be highly expressed, and their codon usage seems to have been shaped by selection favouring a limited number of translationally **optimal** codons. Thus, the frequency of these **optimal** codons in a gene appears to be correlated with the level of gene expression, and may be a useful indicator in the case of genes (or open reading frames) whose expression levels (or even function) are unknown. A second, relatively minor trend among genes is correlated

with the frequency of G at synonymously variable sites. It is not yet clear whether this trend reflects variation in base composition (or mutational biases) among regions of the C.elegans genome, or some other factor. Sequence divergence between C.elegans and C.briggsae has also been studied.

CT Check Tags: Animal; Support, Non-U.S. Gov't
Base Sequence
*Caenorhabditis elegans: GE, genetics
***Codon**
Evolution
Molecular Sequence Data
*Mutation
*Translation, Genetic

CN 0 (Codon)

L135 ANSWER 25 OF 37 MEDLINE
AN 94164953 MEDLINE
DN 94164953
TI An in-frame deletion of codon 298 of the NADH-cytochrome b5 reductase gene results in hereditary methemoglobinemia type II (generalized type). A functional implication for the role of the COOH-terminal region of the enzyme.
AU Shirabe K; Fujimoto Y; Yubisui T; Takeshita M
CS Department of Biochemistry, Oita Medical University, Japan..
SO JOURNAL OF BIOLOGICAL CHEMISTRY, **(1994 Feb 25)** 269 (8) 5952-7.
Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199406
AB The nucleotide sequence was determined for the gene of NADH-cytochrome b5 reductase of a patient of type II hereditary methemoglobinemia found in Yokohama, Japan. An in-frame deletion of 3 base pairs corresponding to codon 298 (TTC) was identified in the patient. The patient was homozygous for the mutation as shown by hybridization experiments using allele-specific oligonucleotides. The mutation causes deletion of Phe-298, which is the third to the COOH-terminal residue, indicating that in this mutant enzyme the sequence of this region has changed from -Cys-Phe-Val-Phe-COOH to -Cys-Val-Phe-COOH. The mutant enzyme, whose Phe-298 was deleted (F298 delta), was prepared by means of a bacterial expression system and site-directed mutagenesis. The kcat/Km value (NADH) of the enzyme was 5.7 s-1 M-1, which corresponds to 0.4% of that of the wild type. Moreover, the enzyme was much less thermostable than the wild type. To examine further the role of the COOH-terminal portion of the enzyme, various mutant enzymes were also prepared and characterized. The enzymatic properties of F298L, F300L, and F298L/F300L were essentially the same as that of the wild type. The kinetic properties of F298A, and F300A were not greatly affected, but the **stability** of the enzymes was somewhat impaired. Since Val-299 is naturally Ala in steer enzyme, no specific residues in the carboxyl-terminal region (298-300) are essential to the enzyme function. The instability of the F298/F300A double mutant indicates that the hydrophobicity of the carboxyl-terminal region of the enzyme might be important to maintain the conformation of the enzyme. high impairment of the activity of the F298 delta, F298stop, and F300stop mutants might be caused by the loss of the residue(s) in the carboxyl-terminal portion. These results indicate that the hydrophobicity, but not the specific amino acid residues, of the carboxyl-terminal portion of the enzyme is important for the **stability** of the enzyme.

CT Check Tags: Human; Male; Support, Non-U.S. Gov't
Adolescence
Amino Acid Sequence
Base Sequence
Catalysis
Circular Dichroism
***Codon**

*Cytochrome Reductases: GE, genetics
Cytochrome Reductases: ME, metabolism
**Enzyme Stability**
Heat
*Methemoglobinemia: GE, genetics
Molecular Sequence Data
Mutation
Oligodeoxyribonucleotides
*Sequence Deletion
CN EC 1.6.2. (Cytochrome Reductases); EC 1.6.2.2 (cytochrome b(5) reductase); 0 (Codon); 0 (Oligodeoxyribonucleotides)

L135 ANSWER 26 OF 37 MEDLINE
AN 93065193 MEDLINE
DN 93065193
TI Evolution of codon usage patterns: the extent and nature of divergence between Candida albicans and Saccharomyces cerevisiae.
AU Lloyd A T; Sharp P M
CS Department of Genetics, Trinity College, Dublin, Ireland..
SO NUCLEIC ACIDS RESEARCH, **(1992 Oct 25)** 20 (20) 5289-95.
Journal code: O8L. ISSN: 0305-1048.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-L00026; GENBANK-M35158; GENBANK-M15867; GENBANK-J05583; GENBANK-M23865; GENBANK-M14760; GENBANK-M30513; GENBANK-M21483; GENBANK-M31132; GENBANK-X53424; GENBANK-X03534; GENBANK-M13358; GENBANK-M63892; GENBANK-X01638; GENBANK-J02706; GENBANK-J01384; GENBANK-K02207; +
EM 199302
AB Codon usage in a sample of 28 genes from the pathogenic yeast Candida albicans has been analysed using multivariate statistical analysis. A major trend among genes, correlated with gene expression level, was identified. We have focussed on the extent and nature of divergence between C.albicans and the closely related yeast Saccharomyces cerevisiae. It was recently suggested that significant differences exist between the subsets of preferred codons in these two species [Brown et al. (1991) Nucleic Acids Res. 19, 4293]. Overall, the genes of C.albicans are more A + T-rich, reflecting the lower genomic G + C content of that species, and presumably resulting from a different pattern of mutational bias. However, in both species highly expressed genes preferentially use the same subset of **'optimal'** codons. A suggestion that the low frequency of NCG codons in both yeast species results from selection against the presence of codons that are potentially highly mutable is discounted. Codon usage in C.albicans, as in other unicellular species, can be interpreted as the result of a balance between the processes of mutational bias and translational selection. Codon usage in two related Candida species, C.maltosa and C.tropicalis, is briefly discussed.
CT Check Tags: Support, Non-U.S. Gov't
*Candida albicans: GE, genetics
***Codon: GE, genetics**
Evolution
*Gene Frequency: GE, genetics
*Genes, Fungal: GE, genetics
Molecular Sequence Data
Repetitive Sequences, Nucleic Acid: GE, genetics
*Saccharomyces cerevisiae: GE, genetics
CN 0 (Codon)

L135 ANSWER 27 OF 37 MEDLINE
AN 92347705 MEDLINE
DN 92347705
TI Polymorphism at codon 72 of the p53 gene in human acute myelogenous leukemia.
AU Zhang W; Hu G; Deisseroth A

CS Department of Hematology, University of Texas M.D. Anderson Cancer Center, Houston 77030.
NC PO1 CA49639-01A1 (NCI)
SO GENE, **(1992 Aug 15)** 117 (2) 271-5.
Journal code: FOP. ISSN: 0378-1119.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199211
AB A common polymorphism at codon 72 of the p53 gene in patients with acute myelogenous leukemia (AML) was analyzed by single-strand conformation polymorphism assay and sodium dodecyl sulfate polyacrylamide-gel electrophoresis of immunoprecipitated 35S-labeled P53 protein. No association between this polymorphism and a marked predisposition to AML was found. The half-lives of these two polymorphic forms of P53 were equivalent in normal phytohemagglutinin-stimulated lymphocytes, while the P53 Pro72 isoform was found to be twice as **stable** as the Arg72 isoform in Daudi cells.
CT Check Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Base Sequence
***Codon: GE, genetics**
DNA, Single-Stranded: GE, genetics
Electrophoresis
*Genes, p53: GE, genetics
*Leukemia, Myelocytic, Acute: GE, genetics
Molecular Sequence Data
Nucleic Acid Conformation
Oligodeoxyribonucleotides: GE, genetics
Polymerase Chain Reaction
*Polymorphism (Genetics): GE, genetics
Tumor Cells, Cultured
CN 0 (Codon); 0 (DNA, Single-Stranded); 0 (Oligodeoxyribonucleotides)
GEN p53

L135 ANSWER 28 OF 37 MEDLINE
AN 92331595 MEDLINE
DN 92331595
TI The 'second-codon rule' and autophosphorylation govern the **stability** and activity of Mos during the meiotic cell cycle in Xenopus oocytes.
AU Nishizawa M; Okazaki K; Furuno N; Watanabe N; Sagata N
CS Division of Molecular Genetics, Kurume University, Fukuoka, Japan..
SO EMBO JOURNAL, **(1992 Jul)** 11 (7) 2433-46.
Journal code: EMB. ISSN: 0261-4189.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199210
AB The c-mos proto-oncogene product, Mos, functions in both early (germinal vesicle breakdown) and late (metaphase II arrest) steps during meiotic maturation in Xenopus oocytes. In the early step, Mos is only partially phosphorylated and metabolically unstable, while in the late step it is fully phosphorylated and highly **stable**. Using a number of Mos mutants expressed in oocytes, we show here that the instability of Mos in the early step is determined primarily by its penultimate N-terminal residue, or by a rule referred to here as the 'second-codon rule'. We demonstrate that unstable Mos is degraded by the ubiquitin-dependent pathway. In the late step, on the other hand, Mos is **stabilized** by autophosphorylation at Ser3, which probably acts to prevent the N-terminus of Mos from being recognized by a ubiquitin-protein ligase. Moreover, we show that Ser3 phosphorylation is essential for Mos to exert its full cytostatic factor (CSF) activity in fully mature oocytes. Thus, a few N-terminal amino acids are primary determinants of both the metabolic **stability** and physiological activity of Mos during the meiotic

cell cycle.
CT Check Tags: Animal; Human; Support, Non-U.S. Gov't
Amino Acid Sequence
Base Sequence
***Codon**
DNA
Electrophoresis, Polyacrylamide Gel
*Meiosis
Molecular Sequence Data
*Ovum: CY, cytology
Peptide Mapping
Phosphorylation
Phosphotransferases: ME, metabolism
Precipitin Tests
Protein-Tyrosine Kinase: GE, genetics
Protein-Tyrosine Kinase: ME, metabolism
*Proto-Oncogene Proteins: GE, genetics
Proto-Oncogene Proteins: ME, metabolism
Serine: ME, metabolism
Ubiquitin: ME, metabolism
Xenopus
RN 56-45-1 (Serine); 9007-49-2 (DNA)
CN EC 2.7 (Phosphotransferases); EC 2.7.1.112 (Protein-Tyrosine Kinase); 0 (Codon); 0 (Proto-Oncogene Proteins c-mos); 0 (Proto-Oncogene Proteins); 0 (Ubiquitin)

L135 ANSWER 29 OF 37 MEDLINE
AN 92223346 MEDLINE
DN 92223346
TI Positional effects on the structure and **stability** of abbreviated H-ras DNA sequences containing O6-methylguanine residues at codon 12.
AU Bishop R E; Moschel R C
CS Chemistry of Carcinogenesis Laboratory, NCI-Frederick Cancer Research and Development Center, Maryland 21702..
NC NO1-CO-74101 (NCI)
SO CHEMICAL RESEARCH IN TOXICOLOGY, **(1991 Nov-Dec)** 4 (6) 647-54.
Journal code: A5X. ISSN: 0893-228X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199207
AB Activation of the H-ras protooncogene in rats by methylating carcinogens results from a G-to-A transition mutation at the second position of codon 12 (GGA), presumably due to formation of an O6-methylguanine (m6G) at this position. A similar transition at the first position of codon 12 appears not to occur in vivo. To study the possible structural basis for this bias in mutation, we synthesized a series of 11-base H-ras sequences [e.g., 5'-d(CGCTG*G*AGGCG)-3' and two complementary strands] containing an m6G at the first, second, or both positions of codon 12 (i.e., G* = m6G). The results of solution chemical studies indicated that the individual strands formed **stable** hairpin structures among which that containing m6G at the second position of codon 12 was most **stable**. Further, the DNA duplex with m6G at the second position was significantly more **stable** than that with m6G at the first position, and under certain conditions, it was more **stable** than the unmodified duplex as well. It is possible that such a difference in **stability** might lead to more ready recognition of an m6G at the first position by repair proteins, and this could contribute to the apparent site specificity of mutation by methylating carcinogens at codon 12 of the H-ras gene.
CT Check Tags: Animal; Support, U.S. Gov't, P.H.S.
Base Sequence
Circular Dichroism
***Codon**
*Genes, ras
*Guanine: AA, analogs & derivatives

Guanine: AN, analysis
Molecular Sequence Data
Rats
RN 20535-83-5 (O-(6)-methylguanine); 73-40-5 (Guanine)
CN 0 (Codon)

L135 ANSWER 30 OF 37 MEDLINE
AN 92205892 MEDLINE
DN 92205892
TI Detection of a rare point mutation in Ki-ras of a human bladder cancer xenograft by polymerase chain reaction and direct sequencing.
AU Grimmond S M; Raghavan D; Russell P J
CS Urological Cancer Research Unit, Royal Prince Alfred Hospital, Sydney, Australia..
SO UROLOGICAL RESEARCH, **(1992)** 20 (2) 121-6.
Journal code: WRX. ISSN: 0300-5623.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199207
AB This paper represents the first report of a codon 59 mutation in Ki-ras from a spontaneous human transitional cell carcinoma of the bladder. Point mutations have the potential to activate the ras genes if they occur in critical coding regions. These include the sequences of codons 12, 13, 59, 61 and 63. Mutations in codons 12, 13 and 61 have been reported in a wide variety of human cancers, including transitional cell carcinoma of the bladder. However mutations in codon 59 have been reported only in retroviral Ki-ras and as a result of in vitro mutagenesis experiments. We have used the polymerase chain reaction and direct sequencing to detect mutations of Ki-ras, and allele-specific restriction analysis to detect mutations of N-ras in xenografts and continuous cell lines established from bladder cancer biopsies of ten different patients as well as in direct biopsy specimens from five human bladder tumours. For studies of Ki-ras, a 139 bp fragment which spanned the critical codons 12 and 13 and a 128 bp fragment that spanned the sequences of codon 59, 61 and 63 were enzymatically amplified and then sequenced. No N-ras mutations were detected. A heterozygous mutation of Ki-ras at codon 59 GCA----G/ACA was detected in one line. This mutation is being expressed and appears **stable** as it was detected over several xenograft passages and was present in paraffin-embedded tissue from the primary tumour of the patient. The biological significance of the mutation in bladder cancer is currently under study.
CT Check Tags: Animal; Human; Support, Non-U.S. Gov't
Base Sequence
*Bladder Neoplasms: GE, genetics
Blotting, Northern
*Carcinoma, Transitional Cell: GE, genetics
***Codon: GE, genetics**
DNA Mutational Analysis
*Genes, ras: GE, genetics
Immunoblotting
Mice
Mice, Inbred BALB C
Molecular Sequence Data
*Mutation: GE, genetics
Polymerase Chain Reaction
Transplantation, Heterologous
CN 0 (Codon)

L135 ANSWER 31 OF 37 MEDLINE
AN 92190477 MEDLINE
DN 92190477
TI Antithrombin-III-Stockholm: a codon 392 (Gly----Asp) mutation with normal heparin binding and impaired serine protease reactivity.
AU Blajchman M A; Fernandez-Rachubinski F; Sheffield W P; Austin R C;

Schulman S
CS Canadian Red Cross Blood Society Transfusion Service, Hamilton, Ontario.
SO BLOOD, **(1992 Mar 15)** 79 (6) 1428-34.
Journal code: A8G. ISSN: 0006-4971.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199206
AB Antithrombin-III-Stockholm is a new structural variant of antithrombin-III (AT-III) with normal heparin affinity but defective serine protease inhibitory activity. The proposita, a white female born in 1966, was diagnosed to have developed a pulmonary embolus while on oral contraceptives at age 19. The proposita, as well as her father, were diagnosed to have a type 2 AT-III deficiency as they had normal levels of immunoreactive AT-III associated with decreased (approximately 60%) functional AT-III when measured with either alpha-thrombin or factor Xa as the substrate, either in the presence or absence of heparin. There was no evidence of abnormal electrophoretic mobility of AT-III from the proposita either in the presence or absence of heparin. Genomic DNA was prepared and all seven AT-III exons were polymerase chain reaction (PCR)-amplified and sequenced in both directions using nested primers. Only exon 7 provided evidence for the presence of a mutation, with the second base of codon 392 having a G----A substitution. Such a mutation would cause the substitution of aspartic acid at the site of the normally appearing glycine in the translated product. Furthermore, this mutation caused the destruction of an Hae III restriction site at this point in the AT-III gene. The absence of this Hae III site was confirmed using restriction fragment length polymorphism analysis of PCR-amplified material from the proposita. Experiments with AT-III from the proposita together with experiments with cell-free translated AT-III-Stockholm provided evidence that the mutant AT-III protein does not efficiently form a **stable** covalent inhibitory complex with alpha-thrombin, although it exhibits normal heparin affinity. The minimal thrombin-complexing ability of the mutant AT-III protein that was observed was accelerated by heparin, but to subnormal levels.
CT Check Tags: Case Report; Female; Human; Support, Non-U.S. Gov't
Adult
*Antithrombin III: GE, genetics
Antithrombin III: ME, metabolism
Base Sequence
***Codon**
Exons
*Heparin: ME, metabolism
Molecular Sequence Data
*Mutation
Polymerase Chain Reaction
*Serine Endopeptidases: AN, analysis
Thrombin: ME, metabolism
RN 9000-94-6 (Antithrombin III); 9005-49-6 (Heparin)
CN EC 3.4.21 (Serine Endopeptidases); EC 3.4.21.5 (Thrombin); 0 (antithrombin III Stockholm); 0 (Codon)

L135 ANSWER 32 OF 37 MEDLINE
AN 92079909 MEDLINE
DN 92079909
TI Codon usage in Aspergillus nidulans.
AU Lloyd A T; Sharp P M
CS Department of Genetics, Trinity College, Dublin, Ireland..
SO MOLECULAR AND GENERAL GENETICS, **(1991 Nov)** 230 (1-2) 288-94.
Journal code: NGP. ISSN: 0026-8925.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199203

AB Synonymous codon usage in genes from the ascomycete (filamentous) fungus Aspergillus nidulans has been investigated. A total of 45 gene sequences has been analysed. Multivariate statistical analysis has been used to identify a single major trend among genes. At one end of this trend are lowly expressed genes, whereas at the other extreme lie genes known or expected to be highly expressed. The major trend is from nearly random codon usage (in the lowly expressed genes) to codon usage that is highly biased towards a set of 19-20 "**optimal**" codons. The G + C content of the A. nidulans genome is close to 50%, indicating little overall mutational bias, and so the codon usage of lowly expressed genes is as expected in the absence of selection pressure at silent sites. Most of the **optimal** codons are C- or G- ending, making highly expressed genes more G + C-rich at silent sites.

CT Check Tags: Support, Non-U.S. Gov't
*Aspergillus nidulans: GE, genetics
Base Composition
***Codon**
Gene Expression
*Genes, Fungal
Open Reading Frames

CN 0 (Codon)

L135 ANSWER 33 OF 37 MEDLINE

AN 91358728 MEDLINE

DN 91358728

TI Four different mutations in codon 28 of alpha spectrin are associated with structurally and functionally abnormal spectrin alpha I/74 in hereditary elliptocytosis.

AU Coetzer T L; Sahr K; Prchal J; Blacklock H; Peterson L; Koler R; Doyle J; Manaster J; Palek J

CS Department of Biomedical Research, St. Elizabeth's Hospital of Boston, Tufts University School of Medicine, Boston, Massachusetts 02135..

NC HL3746 (NHLBI)
HL27215 (NHLBI)

SO JOURNAL OF CLINICAL INVESTIGATION, **(1991 Sep)** 88 (3) 743-9.
Journal code: HS7. ISSN: 0021-9738.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals

EM 199112

AB Hereditary elliptocytosis (HE) Sp alpha I/74 is a disorder associated with defective spectrin (Sp) heterodimer self-association and an abnormal tryptic cleavage of the 80-kD alpha I domain of Sp resulting in increased amounts of a 74-kD peptide. The molecular basis of this disorder is heterogeneous and mutations in codons 28, 46, 48, and 49 (codons 22, 40, 42, and 43 in the previous nomenclature which did not include the six NH2-terminal amino acids) have been reported. In this study we present data on seven unrelated HE Sp alpha I/74 kindred from diverse racial backgrounds in whom we identified four different mutations all occurring in exon 2 of alpha Sp at codon 28. Utilizing the polymerase chain reaction we established a CGT----CTT; Arg----Leu 28 mutation in one kindred of Arab/Druze origin. In two unrelated white kindred of English/European origin the substitution is CGT----AGT; Arg----Ser 28 and in two apparently unrelated white kindred from New Zealand, the mutation is CGT----TGT; Arg----Cys 28. Finally, in one American black kindred and in a black kindred from Ghana the mutation involves CGT----CAT; Arg----His 28. Allele specific oligonucleotide hybridization confirmed that the probands are heterozygous for the respective mutant alleles. All four point mutations abolished an Aha II restriction enzyme site which allowed verification of linkage of the mutation with HE Sp alpha I/74. Our results imply that codon 28 of alpha Sp is a "hot spot" for mutations and also indicate that Arg 28 is critical for the conformational **stability** and functional self association of Sp heterodimers.

CT Check Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Base Sequence

*Codon
*Elliptocytosis, Hereditary: GE, genetics
Linkage (Genetics)
Molecular Sequence Data
*Mutation
Nucleic Acid Hybridization
Polymorphism, Restriction Fragment Length
Protein Conformation
*Spectrin: GE, genetics
RN 12634-43-4 (Spectrin)
CN 0 (Codon)

L135 ANSWER 34 OF 37 MEDLINE
AN 91355581 MEDLINE
DN 91355581
TI Synthesis, characterization, and solution properties of ras sequences modified by arylamine carcinogens at the first base of codon 61.
AU Marques M M; Beland F A
CS Centro de Quimica Estrutural, Complexo I, I.S.T., Lisboa, Portugal..
SO CHEMICAL RESEARCH IN TOXICOLOGY, **(1990 Nov-Dec)** 3 (6) 559-65.
Journal code: A5X. ISSN: 0893-228X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199112
AB The complementary pentadecamers d(5'-TACTCTTCTTGACCT) (strand A) and d(5'-AGGTCAAGAAGAGTA) (strand B), which span a portion of the mouse c-Ha-ras protooncogene centered around codon 61, were synthesized by using standard beta-cyanoethyl phosphoramidite chemistry and characterized by sequence analysis. Strand A, containing a sole guanine at the position corresponding to the first base of codon 61, was modified with N-acetoxy-N-(trifluoroacetyl)-2-aminofluorene or its 4-aminobiphenyl analogue. In both cases only the corresponding N-(deoxyguanosin-8-yl)arylamine adduct was formed, as judged from HPLC and UV analyses conducted after enzymatic hydrolysis of the modified oligomers. Nonmodified and modified pentadecamers were annealed with strand B. Cooperative melting transitions were observed with all samples, thus indicating the formation of **stable** duplexes. Melting temperatures decreased in the order nonmodified duplex greater than 2-aminofluorene-modified duplex greater than 4-aminobiphenyl-modified duplex, which indicated destabilization of the helical structure upon incorporation of the adducts, with 4-aminobiphenyl having the greatest effect. Circular dichroism spectra of all duplexes were characteristic of an overall right-handed B-type conformation, with no major conformational differences being detected between the two arylamine-modified oligomers.
CT *Aminobiphenyl Compounds: ME, metabolism
Base Sequence
*Carcinogens: ME, metabolism
Circular Dichroism
*Codon
*Fluorenes: ME, metabolism
*Genes, ras
Molecular Sequence Data
Oligonucleotides: ME, metabolism
RN 153-78-6 (2-aminofluorene); 90-41-5 (2-aminodiphenyl)
CN 0 (Aminobiphenyl Compounds); 0 (Carcinogens); 0 (Codon); 0 (Fluorenes); 0 (Oligonucleotides)

L135 ANSWER 35 OF 37 MEDLINE
AN 91136596 MEDLINE
DN 91136596
TI [Rare initiation codons are regulators of expression of the rpoC gene (letter)].
Redkie initsiiruiushchie kodony-reguliatory ekspressii gena rpoC.
AU Boni I V; Borodin A M

SO BIOORGANICHESKAIA KHIMIIA, **(1990 Aug)** 16 (8) 1134-7.
Journal code: 9Z8. ISSN: 0132-3423.
CY USSR
DT Letter
LA Russian
FS Priority Journals
EM 199105
AB Translation of the rpoC genes in Escherichia coli and Salmonella typhimurium is known to start from the GUG codon. Now, using toeprint analysis we have shown UUG to be the initiation codon of the Pseudomonas putida rpoC gene. IF3 does not seem to proofread initiation at the UUG codon. The rpoC genes of P. putida, E. coli, and S. typhimurium, which use rare start codons, have strong SD-domains AGGAGG (P. p.) and GGGAG (E. c., S. t.), **optimal** seven-nucleotide spacing between SD and start codons, and good second codon AAA. We suggest that rpoC presents an infrequent case of the regulation of translation initiation by selecting the start codon.
CT Base Sequence
***Codon**
English Abstract
Escherichia coli: GE, genetics
*Gene Expression Regulation, Bacterial
Molecular Sequence Data
Pseudomonas: GE, genetics
Salmonella typhimurium: GE, genetics
Translation, Genetic
CN 0 (Codon)
GEN rpoC

L135 ANSWER 36 OF 37 MEDLINE
AN 91033053 MEDLINE
DN 91033053
TI CUG as a mutant start codon for cat-86 and xylE in Bacillus subtilis.
AU Ambulos N P Jr; Smith T; Mulbry W; Lovett P S
CS Department of Biological Sciences, University of Maryland Baltimore County, Catonsville 21228.
NC GM42925 (NIGMS)
SO GENE, **(1990 Sep 28)** 94 (1) 125-8.
Journal code: FOP. ISSN: 0378-1119.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199102
AB The cat-86 gene specifies chloramphenicol acetyltransferase (CAT). The cat-86 start codon is UUG, although related genes have AUG as the start codon. Changing the start codon to AUG increased expression of cat-86 by 36% in Bacillus subtilis. Changing the start codon to GUG and CUG decreased expression to 65% and 30%, respectively, of the level obtained when AUG was the start codon. CUG has not been previously shown to function as a start codon in B. subtilis. N-terminal sequencing of purified CAT protein specified by the CUG mutant, revealed that CUG was indeed the start codon and specified methionine. The gene xylE, which specifies catechol 2,3-dioxygenase, has AUG as its start codon. Changing the start codon for xylE to CUG decreased expression by 98%. However, when the ribosome-binding site sequence for xylE was **optimized** and the spacing between it and the start codon was increased to 8 nucleotides, xylE activity increased to 13% of the activity observed for AUG. CUG did not function efficiently as a start codon for cat-86 in Escherichia coli. These data suggest conditions under which CUG can function, with modest efficiency, as a start codon in B. subtilis.
CT Check Tags: Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.
Bacillus subtilis: EN, enzymology
*Bacillus subtilis: GE, genetics
Base Sequence
Calorimetry

*Chloramphenicol O-Acetyltransferase: GE, genetics
***Codon: GE, genetics**
*Genes, Bacterial
Molecular Sequence Data
*Mutagenesis, Site-Directed
Polymerase Chain Reaction
Translation, Genetic
CN EC 2.3.1.28 (Chloramphenicol O-Acetyltransferase); 0 (Codon)
GEN cat-86; xylE

L135 ANSWER 37 OF 37 MEDLINE
AN 91012600 MEDLINE
DN 91012600
TI Switches in species-specific codon preferences: the influence of mutation biases.
AU Shields D C
CS Department of Genetics, Trinity College, Dublin, Ireland..
SO JOURNAL OF MOLECULAR EVOLUTION, **(1990 Aug)** 31 (2) 71-80. Ref: 31
Journal code: J76. ISSN: 0022-2844.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199101
AB A model of synonymous codon usage is developed in which the most frequent codons are selectively advantageous because of their coadaptation with tRNA abundances. Random drift opposes the progress of this coevolution by pushing codon frequencies in the direction of the frequency that would result from mutation in the absence of selection. It is predicted that, within a certain range, an increased mutation bias away from an advantageous codon has little influence on its usage in highly expressed genes. However, a subsequent small increase in mutation bias over a critical range leads to a large reduction in the frequency of the codon. The switch in preference from one synonym to another is a sharp transition, with no **stable** intermediate state in which neither codon is advantageous. Codon usage patterns were compared among three related bacterial species of differing genomic G & C contents, Escherichia coli, Serratia marcescens, and Proteus vulgaris. It was found that although changes in mutation biases do not always result in switches in codon preferences, some switches have occurred in the direction of species-specific mutation biases. Fluctuating mutation biases may therefore be the main cause of differences between species in their codon preferences.
CT Amino Acids: AN, analysis
Base Composition
***Codon**
*Enterobacteriaceae: GE, genetics
*Mutation
*Selection (Genetics)
Species Specificity
CN 0 (Amino Acids); 0 (Codon)